Antiphospholipid antibody-related clinical manifestations during childhood *versus* adulthood: descriptive results from the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) clinical database and repository

J. Pandya Bhatt[1], M. Dale[2], D.C.O. de Andrade[3], A.E. Clarke[4], M.G. Tektonidou[5], V. Pengo[6], S. Sciascia[7], J. Pardos-Gea[8], M.A. Aguirre-Zamorano[9], N. Kello[10], D. Paredes-Ruiz[11], H.M. Belmont[12], P.R. Fortin[13], D. Wahl[14], W. Branch[15], M. Gerosa[16], G. de Jesus[17], Z. Zhang[18], T. Atsumi[19], M. Efthymiou[20], G. Pazzola[21], C. Nalli[22], A. Duarte-García[23], E. Rodriguez Almaraz[24], M. Petri[25], R. Cervera[26], B. Artim-Esen[27], G. Pons-Estel[28], H. Shi[29], Y. Zuo[30], R. Willis[31], M.R.W. Barber[4], L. Skeith[4], M. Radin[7], A. Anunciacion-Llunell[8], M.L. Bertolaccini[32], H. Cohen[20], D. Erkan[33]

Abstract

Objective

There is a limited number of studies comparing paediatric to adult antiphospholipid syndrome (APS) patients. Our objective was to analyse the characteristics of patients presenting with antiphospholipid antibody (aPL)-related clinical manifestations during childhood versus adulthood.

Methods

We retrieved baseline characteristics from an international registry of persistently aPL-positive adult patients. Clinical events were grouped as vascular and non-vascular. We compared the frequency of and the timeline between vascular and non-vascular events for different age groups at the time of their first aPL-related manifestations: a) paediatric- (0–17 years) versus adult-onset (18–75 years); and b) based on narrower age intervals. Secondly, we analysed the timeline between the first aPL-related clinical event and first aPL positivity.

Results

Of 787 patients, 447 (57%) had only vascular events, 108 (14%) only non-vascular events, and 232 (29%) both. Compared to adult-onset patients (n=742), paediatric-onset patients (n=45) presented more commonly with a non-vascular event (49% vs. 19%, p=0.0001). The percentage of patients presenting with a non-vascular event mostly decreased with each increasing age group. Timeline analysis demonstrated 317 (40%) patients had a positive aPL test within the same calendar year (c-y) of the first clinical event, 207 (26%) within 1 to 3 c-y, and 263 (33%) more than 3 c-y.

Conclusion

Our analysis of an international registry for persistently aPL-positive patients demonstrates that patients with paediatric-onset aPL-related manifestations more commonly present with non-vascular events. These results highlight the importance of understanding the clinical differences between paediatric and adult APS patients, which have diagnostic, therapeutic, and research implications.

Key words

antiphospholipid antibodies, antiphospholipid syndrome, paediatric antiphospholipid syndrome

Affiliations on page 91.

Jheel Pandya Bhatt, MD
Marissa Dale, MD
Danieli Castro Oliveira de Andrade, MD
Ann E. Clarke, MD
Maria G. Tektonidou, MD, PhD
Vittorio Pengo, MD
Savino Sciascia, MD, PhD
Jose Pardos-Gea, MD
M. Angeles Aguirre-Zamorano, MD
Nina Kello, MD
Diana Paredes-Ruiz, MD
H. Michael Belmont, MD
Paul R. Fortin, MD
Denis Wahl, MD
Ware Branch, MD
Maria Gerosa, MD, PhD
Guilherme de Jesus, MD
Zhuoli Zhang, MD
Tatsuya Atsumi, MD
Maria Efthymiou, PhD
Giulia Pazzola, MD
Cecilia Nalli, MD
Alí Duarte-García, MD
Esther Rodriguez Almaraz, MD
Michelle Petri, MD, MPH
Ricard Cervera, MD
Bahar Artim-Esen, MD
Guillermo Pons-Estel, MD
Hui Shi, MD
Yu Zuo, MD, PhD
Rohan Willis, MD
Megan R.W. Barber, MD
Leslie Skeith, MD
Massimo Radin, MD
Ariadna Anunciacion-Llunell, MD
Maria Laura Bertolaccini, PhD
Hannah Cohen, MD
Doruk Erkan, MD, MPH

Please address correspondence to:
Doruk Erkan
Hospital for Special Surgery,
535 East 70th Street,
New York, NY 10021, USA.
E-mail: erkand@hss.edu

Received on March 23, 2025; accepted in revised form on July 2, 2025.

Competing interests: see page 91.

Introduction

Antiphospholipid syndrome (APS) is a systemic autoimmune disorder caused by antibodies against phospholipid-binding plasma proteins (antiphospholipid antibodies [aPL]), mainly lupus anticoagulant test (LA), anticardiolipin antibodies (aCL), and anti-β_2-glycoprotein-I antibodies (aβ_2GPI). Traditionally, APS diagnosis and classification focused on moderate-to-large vessel thrombosis and obstetric complications. However, aPL can be associated with a wide range of microvascular and non-thrombotic manifestations (1, 2) such as skin (*e.g.* livedo reticularis/racemosa and cutaneous ulcers), renal (aPL-nephropathy), cardiac valve disease (thickening and vegetations), and haematologic (thrombocytopenia and haemolytic anaemia) (2, 3).

Systemic autoimmune rheumatic diseases (SARDs) present differently in different age groups (4). Several paediatric APS small-scale studies also have highlighted the importance of early recognition of the non-thrombotic aPL manifestations, as they may more commonly be the initial presentation, when compared to adults (1, 4-7), and can significantly impact the quality of life and overall health outcomes of affected paediatric APS patients (8, 9).

The Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) was created in 2010 to conduct large-scale multicentre clinical studies and trials in persistently aPL-positive patients. The goal of the APS ACTION Clinical Database and Repository ("Registry") is to study the natural course of persistently aPL-positive patients with or without other SARDs over at least 10 years (10). Given the limited knowledge regarding the presentation of aPL-positive paediatric patients *versus* adult patients, the aim of this study was to analyse the characteristics of patients presenting with aPL-related clinical manifestations during childhood (paediatric-onset) *versus* adulthood (adult-onset).

Methods

The APS ACTION Registry includes adults aged 18–75 who have tested positive for aPL, with or without a formal APS diagnosis, based on the laboratory component of the Revised Sapporo Classification Criteria, confirmed at least twice within one year prior to enrollment (11). For this retrospective analysis, we retrieved baseline demographic, clinical (including the first aPL-related event type/date [paediatric- *vs*. adult- onset]), and laboratory (including the first centre-reported positive aPL date [paediatric- *vs*. adult-onset]) characteristics of patients. Data regarding paediatric aPL history were obtained retrospectively, as all participants were adults at the time of registry entry. Events were grouped as: vascular (arterial, venous, microvascular, catastrophic, superficial vascular, and transient ischaemic attack [TIA]); and non-vascular (immune thrombocytopenia, autoimmune haemolytic anaemia [AIHA], cardiac valve disease, and cognitive dysfunction). Thrombocytopenia was defined as a platelet count of <100 x 10^9/L tested twice at least 12 weeks apart, and AIHA as persistent anaemia with haemolysis and a positive direct antiglobulin test. Cardiac valve disease was recorded based on the definitions included in the Revised Sapporo APS Classification Criteria publication (11), and cognitive dysfunction was recorded only if supported by the neuropsychiatric testing. Of note, obstetric aPL-related manifestations were not included in the analysis. For aPL profile assessment, we defined aCL and aβ_2GPI IgG/M as 'positive' when the reported titre was ≥40 Units on enzyme-linked immunosorbent assays (ELISA).

First, we compared the frequency of and the timeline between vascular and non-vascular events for patients in different age groups at the time of their first aPL-related manifestations: a) paediatric- (0–17 years) *versus* adult-onset (18–75 years); and b) based on narrower age intervals, which were: 0–10 years, 11–17 years, 18–30 years, 31–40 years, 41-50 years, 51–60 years, 61–70 years and 71–75 years (the upper limit for age for inclusion in the registry has been 75 years). Secondly, we analysed the timeline between the first aPL-related clinical event and first aPL positivity.

Data were generally analysed descrip-

tively. Count measures were summarised as frequency and percentages. Continuous measures were summarised as mean and standard deviation; t-test was used for group comparisons. Categorical variables were compared using chi-square or Fisher's exact test, where appropriate. *p*-values ≤0.05 were considered statistically significant.

Results

Among 1,122 patients recruited as of January 2023, 335 (30%) were excluded due to no history of an aPL-related event. The mean age of the remaining 787 patients at registry entry was 46 years ± 14 (70% [547] female; 61% (484) had no other SARDs, and 32% [248] fulfilled 1997 ACR SLE classification criteria); 447 (57%) had only vascular events, 108 (14%) only non-vascular events, and 232 (29%) both. The distribution of 403 non-vascular events overall was 205 (51%) for immune thrombocytopenia, 103 (26%) for cardiac valve disease, 58 (14%) AIHA, and/or 37 (9%) cognitive dysfunction (some patients had more than one non-vascular event).

There was no major difference between the demographic and aPL characteristics of the patients except adult-onset patients were older at the registry entry and were more likely to be female. Regarding the clinical characteristics, paediatric-onset patients presented more commonly with a non-vascular event (as the first or only event), compared to adult-onset patients (49% *vs.* 19%, *p*=0.0001) (Table I). Of 22 paediatric patients with non-vascular events as the first event, 17 (77%) had immune thrombocytopenia, six (27%) AIHA, three (14%) cognitive dysfunction, and/or two (9%) cardiac valve disease (some patients had overlapping events). The percentage of patients presenting with a non-vascular event as the first event mostly decreased with each increasing age group except the ages 61–70 (Table II, Fig. 1), ranging from 71% for ages 0–10 to 10% for ages 71–75. A subgroup analysis of 484 aPL-positive patients with no other SARDs, revealed no significant change in the results; 47% of paediatric-onset and 20% of adult-onset patients presented with a non-vascular event (*p*=0.0007, full data not shown).

Table I. Antiphospholipid antibody-related clinical manifestations during childhood versus adulthood: descriptive results from the APS ACTION Clinical Database and Repository ("Registry").

First clinical event age group (no. of patients, %)	Paediatric-onset (ages 0–17) n=45	Adult-onset (ages 18–75) n=742	*p*-value
Demographics			
Mean age (Registry entry)	30.4 ± 10.4	47.2 ± 10.2	<0.0001
Female	23 (51%)	524 (71%)	0.006
White	34 (76%)	496 (67%)	0.79
Antiphospholipid antibody profile			
Lupus anticoagulant positive	40/45 (89%)	596/726 (82%)	0.31
aCL IgG positive	31/45 (69%)	411/714 (58%)	0.16
aCL IgM positive	10/39 (26%)	132/655 (20%)	0.41
aβ_2GPI IgG positive	25/44 (57%)	328/692 (47%)	0.27
aβ_2GPI IgM positive	9/44 (21%)	108/623 (17%)	0.54
Vascular events (VE) only	14 (31%)	433 (58%)	0.0003
Vascular & Non-vascular events (NVE)	19 (42%)	213 (29%)	0.06
VE more than one calendar year (c-y) prior to NVE	8	96	
VE and NVE within the same c-y	1	69	
NVE more than one c-y prior to VE	10	48	
Non-vascular events only	12 (27%)	96 (13%)	0.02
Vascular events (total)	33 (73%)	646 (87%)	0.02
Non-vascular events (total)*	31 (69%)	309 (42%)	0.0005
Vascular events (as the first event)**	22 (49%)	529 (70%)	0.0023
Non-vascular events (as the first event)**	22 (49%)	144 (19%)	0.0001

*Chorea was reported in 1/45 (2%) and 13/742 (2%) of paediatric- and adult-onset patients, respectively; seizure disorder was reported in 2/45 (4%) and 81/742 (11`%) of paediatric- and adult-onset patients, respectively (not included in the analysis given the lack of onset date in the registry).
**Patients with vascular and non-vascular events within the same calendar year were excluded.

Timeline analysis between the first aPL event and aPL positivity demonstrated that 317 (40%) patients had a positive aPL test within the same calendar year (c-y) of the first clinical event, 207 (26%) within (±) 1 to 3 c-y, and 263 (33%) more than (±) 3 c-y.

Discussion

Our analysis of a large-scale international multicentre registry for persistently aPL-positive patients demonstrates that patients with paediatric-onset aPL-related manifestations more commonly present with non-vascular events than adult-onset aPL-related manifestations.

Previous studies have shown that many paediatric patients exhibit non-vascular manifestations at the time of their first thrombotic event. The Peds-APS Registry, which is one of the largest paediatric APS cohorts to date with 121 patients, reported a high prevalence of non-thrombotic clinical features, including haematologic disorders, skin manifestations, and neurologic issues (1). Ma *et al*. also identified frequent non-thrombotic manifestations in their cohort of 58 paediatric APS patients, with immunologic thrombocytopenia and AIHA being the most common (6). Morán-Álvarez *et al*. found a high frequency of haematologic manifestations in their multicentre cohort of aPL-positive paediatric patients, and over 90% of paediatric patients with positive aPL did not experience a thrombotic event during follow-up (12). Baleeiro *et al*. found a higher frequency of skin ulcers in their youth-onset primary APS patients compared to those with adult-onset primary APS (13). While most paediatric APS studies have focused on non-vascular manifestations occurring alongside the initial thrombotic event, non-vascular manifestations can also present as the initial or only signs of paediatric APS (12, 14). In our cohort of paediatric-onset patients, we found that nearly half of patients presented with a non-vascular event as their initial clinical sign of paediatric APS. This finding highlights the need for greater awareness that, particularly in children,

Table II. Description of vascular and non-vascular events for 787 patients included in the APS ACTION registry, by age groups.

First clinical event age group (no. of patients, %)	0-10 n=7	11–17 n=38	18-30 n=253	31–40 n=188	41–50 n=165	51–60 n=83	61–70 n=43	71–75 n=10	Total n=787
Vascular events (VE) only	1 (14%)	13 (34%)	14 (57%)	102 (54%)	10 (64%)	55 (66%)	24 (56%)	4 (40%)	**447**
VE & Non-vascular events (NVE)	4 (57%)	15 (39%)	74 (29%)	58 (31%)	39 (24%)	23 (28%)	14 (33%)	5 (50%)	**232**
• VE more than one calendar year (c-y) prior to NVE	1	7	37	24	16	14	4	1	**104**
• VE and NVE within the same c-y	0	1	18	23	14	6	4	4	**70**
• NVE more than one c-y prior to VE	3	7	19	11	9	3	6	0	**58**
Non-vascular events only	2 (29%)	10 (26%)	36 (14%)	28 (15%)	21 (13%)	5 (6%)	5 (12%)	1 (10%)	**108**
Vascular events (total)	5 (71%)	28 (74%)	217 (86%)	160 (85%)	144 (87%)	78 (94%)	38 (88%)	9 (90%)	**679**
Non-vascular events (total)	6 (86%)	25 (66%)	110 (43%)	86 (46%)	60 (36%)	28 (34%)	19 (44%)	6 (60%)	**340**
Vascular events (as the first event)*	2 (29%)	20 (53%)	180 (71%)	126 (67%)	121 (73%)	69 (83%)	28 (65%)	5 (50%)	**551**
Non-vascular events (as the first event)*	5 (71%)	17 (45%)	55 (22%)	39 (21%)	30 (18%)	8 (10%)	11 (26%)	1 (10%)	**166**

*Patients with vascular and non-vascular events within the same calendar year were excluded.

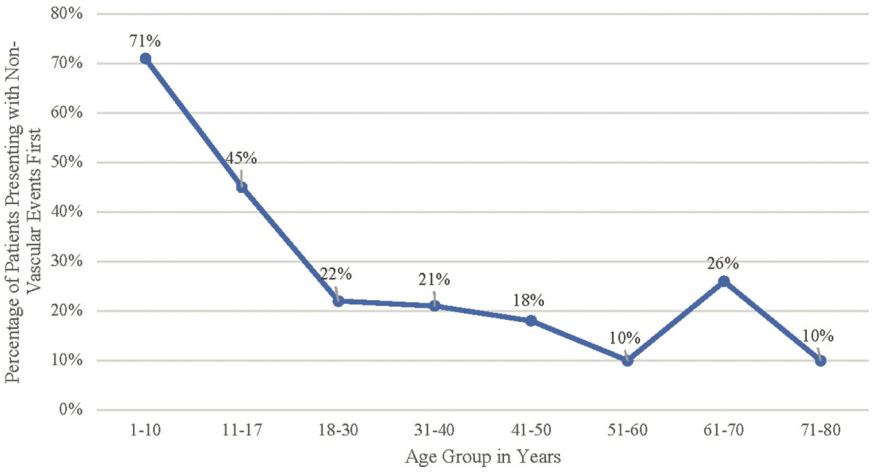

Fig. 1. Percentage of patients presenting with non-vascular events first, by age groups.
*Refer to Table II for the number of patients per age group.

non-vascular manifestations may precede the occurrence of thrombosis.

Antiphospholipid syndrome most often presents in young adults before the fifth decade of life (15). Although less widely studied, APS has also been described in elderly patients (15, 16). Cervera *et al*. reported that patients with older-onset APS, defined as 50 years and older, experienced higher rates of stroke and angina pectoris (3). Similarly, Masson *et al*. found that elderly APS patients, defined as over 65 years old, had a higher incidence of myocardial infarctions and lower limb deep vein thrombosis compared to younger patients (17). Although APS is a relatively rare cause of stroke in the elderly, several case reports have highlighted the importance of considering APS in cases of recurrent stroke in the elderly population (18, 19). Our study demonstrated the frequency of vascular events at the time of initial APS presentation generally increases with age, while the frequency of non-vascular events decreases.

To our knowledge, this is the first study utilising an international large-scale database to understand the differences in presentation of aPL-related manifestations between paediatric and adult aged patients. However, there are several limitations to our study. A key limitation of our study is its retrospective nature, increasing potential for recall bias and incomplete childhood medical history. We were also unable to incorporate some additional non-vascular aPL-related manifestations such as chorea and seizures due to lack of available event dates in the registry. Furthermore, the registry did not collect data on LA-hypoprothrombinaemia syndrome, which is more common in paediatric APS patients. It is also important to note that aPL-related events occurring within the same calendar year but several months apart were included in the group of events occurring at the same time/year in order to have a clear distinction between the first and the subsequent events. The patients were also analysed based on the age at first clinical event; therefore, if they had more than one type of vascular or non-vascular event at different ages, only the youngest age at presentation was included in the data. Given that our time analysis was limited to the initial aPL-related manifestation, conclusions regarding disease progression and subsequent clinical features cannot be drawn. Longitudinal and prospective research is warranted to better define the natural history of disease, particularly in paediatric cohorts. In addition, most of the centres included in the APS ACTION registry are adult hospitals or tertiary care institutions, which may limit the generalisability of the results.

In conclusion, our analysis of a large-scale international multicentre registry revealed significant differences in the first presentation of APS between pae-

diatric and adult-onset patients. These findings have research implications; and highlight the need for age-specific diagnostic strategies in APS, especially in paediatric patients as the presence of non-vascular manifestations may provide key clues to earlier disease diagnosis.

Acknowledgments
The APS ACTION Registry was created using REDCap provided by the Clinical and Translational Science Center at Weill Cornell Medical College (CTSC grant UL1 TR000457). We want to thank JoAnn Vega, CCRC, for her administrative support as the APS ACTION Global Lead Coordinator. We also want to thank all our APS ACTION Members: Guillermo Pons-Estel (Santa Fe, Argentina); Bill Giannakopoulos, Steve Krilis (Sydney, Australia); Guilherme de Jesus, Roger Levy, Flavio Signorelli (Rio de Janeiro, Brazil), Danieli Andrade, Gustavo Balbi (Sao Paulo, Brazil); Ann E. Clarke, Leslie Skeith (Calgary, Canada), Paul R. Fortin (Quebec City, Canada); Lanlan Ji, Zhouli Zhang (Beijing, China), Chengde Yang, Hui Shi (Shanghai, China); Cecile Yelnik (Lilly, France), Stephane Zuily, Denis Wahl (Nancy, France); Maria G. Tektonidou (Athens, Greece); Cecilia Nalli, Laura Andreoli, Angela Tincani (Brescia, Italy), Cecilia B. Chighizola, Maria Gerosa, Pierluigi Meroni (Milan, Italy), Vittorio Pengo (Padova, Italy), Giulia Pazzola (Reggio Emilia, Italy), Savino Sciascia, Silvia Foddai, Massimo Radin (Turin, Italy); Stacy Davis (Kingston, Jamaica); Olga Amengual, Tatsuya Atsumi (Sapporo, Japan); Imad Uthman (Beirut, Lebanon); Maarten Limper, Philip de Groot (Utrecht, The Netherlands); Guillermo Ruiz-Irastorza (Barakaldo, Spain), Ignasi Rodriguez-Pinto, Ricard Cervera, Jose Pardos-Gea (Barcelona, Spain), Esther Rodriguez Almaraz (Madrid, Spain), Maria Angeles Aguirre Zamorano, Chary Lopez-Pedrera (Cordoba, Spain); Bahar Artim-Esen (Istanbul, Turkey); Maria Laura Bertolaccini, Hannah Cohen, Maria Efthymiou, Ian Mackie, Giovanni Sanna (London, UK); Jason Knight, Yu Zuo (Ann Arbor, MI, USA), Michelle Petri (Baltimore, MD, USA), Rebecca K. Leaf (Boston, MA, USA), Elena Gkrouzman (Worcester, MA, USA), Robert Roubey (Chapel Hill, NC, USA), Thomas Ortel (Durham, NC, USA), Emilio Gonzalez, Rohan Willis (Galveston, Texas, USA), Nina Kello (New Hyde Park, NY, USA), Michael Belmont, Medha Barbhaiya, Doruk Erkan, Steven Levine, Michael Lockshin, Jacob Rand, Jane Salmon (New York City, NY, USA), Ali A. Duarte Garcia (Rochester, MN, USA), D. Ware Branch (Salt Lake City, UT, USA), and Nicola Pozzi (St Louis, MO, USA).

Competing interests
V. Pengo has received lecture fees from Werfen, Italy; W. Branch has received reseach funding from UCB Pharma; T. Atsumi has received consultancy fees and grant/research support from MBI and Werfen; R. Cervera has received consultancy fees from Roche; L. Skeith has received honoraria from CSL Behring, Leo Pharma and Sanofi, and research support from CSL Behring; H. Cohen has received consultancy fees from UCB Biopharma and Roche, lecture fees from Technoclone and GSK, and is an Advisory Board member for Roche, argenx and Roche.
The other authors have declared no competing interests.

Affiliations
[1]AdventHealth for Children, Orlando, USA;
[2]Hospital for Special Surgery, New York, NY, USA;
[3]University of São Paulo, Brazil;
[4]University of Calgary, Alberta, Canada;
[5]National and Kapodistrian University of Athens, Greece;
[6]Padova University Hospital, Italy;
[7]ASL Città Di Torino and University of Turin, Italy;
[8]Vall d'Hebron University Hospital Barcelona, Spain;
[9]IMIBIC/Reina Sofia Hospital, University of Cordoba, Spain;
[10]Northwell Health, Great Neck, NY, USA;
[11]Biobizkaia Health Research Institute, Barakaldo, Spain;
[12]New York University Langone Medical Center, New York, NY, USA;
[13]CHU de Québec-Université Laval, Quebec, Canada;
[14]Université de Lorraine, Inserm DCAC, and CHRU-Nancy, France;
[15]University of Utah and Intermountain Healthcare, Salt Lake City, UT, USA;
[16]University of Milan, Italy;
[17]Universidade do Estado do Rio de Janeiro, Brazil;
[18]Peking University First Hospital, Beijing, China;
[19]Hokkaido University Hospital, Sapporo, Japan;
[20]University College London, UK;
[21]Rheumatology Unit, Azienda USL IRCCS di Reggio Emilia, Italy;
[22]University of Brescia, Italy;
[23]Mayo Clinic, Rochester, MN, USA;
[24]Hospital Universitario 12 de Octubre, Madrid, Spain;
[25]Johns Hopkins University School of Medicine, Baltimore, MD, USA;
[26]Hospital Clinic Barcelona, Spain;
[27]Istanbul University School of Medicine, Istanbul, Turkey;
[28]Centro Regional de Enfermedades Autoinmunes y Reumáticas del Grupo Oroño (GO-CREAR), Rosario, Argentina;
[29]Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China;
[30]University of Michigan, Ann Arbor, MI, USA;
[31]University of Texas Medical Branch, Galveston, TX, USA;
[32]King's College London, UK;
[33]Barbara Volcker Center for Women and Rheumatic Disease, Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, USA.

References
1. AVCIN T, CIMAZ R, SILVERMAN ED *et al.*: Pediatric antiphospholipid syndrome: clinical and immunologic features of 121 patients in an international registry. *Pediatrics* 2008; 122(5): 1100-7. https://doi.org/10.1542/peds.2008-1209
2. BARBHAIYA M, ZUILY S, NADEN R *et al.*: 2023 ACR/EULAR antiphospholipid syndrome classification criteria. *Ann Rheum Dis* 2023; 82 (10): 1258-70. https://doi.org/10.1136/ard-2023-224609
3. CERVERA R, PIETTE JC, FONT J *et al.*: Antiphospholipid syndrome: clinical and immunologic manifestations and patterns of disease expression in a cohort of 1,000 patients. *Arthritis Rheum*; 2002. 46(4): 1019-27. https://doi.org/10.1002/art.10187
4. RADIN M, CECCHI I, ARBRILE M *et al.*:

Pediatric presentation of antiphospholipid syndrome: a review of recent literature with estimation of local prevalence. *Semin Thromb Hemost* 2023; 50(2): 182-87. https://doi.org/10.1055/s-0043-1764472.

5. BITSADZE V, KHIZROEVA J, LAZARCHUK A *et al*.: Pediatric antiphospholipid syndrome: is it the same as an adult? *J Matern Fetal Neonatal Med* 2024; 37(1). https://doi.org/10.1080/14767058.2024.2390637
6. MA J, SONG H, WEI M, HE Y: Clinical characteristics and thrombosis outcomes of paediatric antiphospholipid syndrome: analysis of 58 patients. *Clin Rheumatol* 2018; 37(5): 1295-303. https://doi.org/10.1007/s10067-017-3776-5
7. MADISON JA, GOCKMAN K, HOY C, TAMBRALLI A, ZUO Y, KNIGHT JS: Pediatric antiphospholipid syndrome: clinical features and therapeutic interventions in a single center retrospective case series. *Pediatr Rheumatol Online J* 2022; 20(1). https://doi.org/10.1186/s12969-022-00677-8
8. TORRES-JIMENEZ A-R, RAMIREZ-NOVA V, CESPEDES-CRUZ AI *et al*.: Primary antiphospholipid syndrome in pediatrics: beyond thrombosis. report of 32 cases and review of the evidence. *Pediatr Rheumatol Online J* 2022; 20(1). https://doi.org/10.1186/s12969-022-00673-y
9. ZAJC AVRAMOVIC M, AVCIN T: Antiphospholipid syndrome in children. *Best Pract Res Clin Rheumatol* 2024; 38(3). https://doi.org/10.1016/j.berh.2024.101986
10. ERKAN D, LOCKSHIN M *et al*.: APS ACTION – AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking. *Lupus* 2012; 21(7): 695-98. https://doi.org/10.1177/0961203312437810
11. MIYAKIS S, LOCKSHIN MD, ATSUMI T *et al*.: International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006; 4(2): 295-306. https://doi.org/10.1111/j.1538-7836.2006.01753.x
12. MORÁN-ÁLVAREZ P, ANDREU-SUÁREZ L, CABALLERO-MOTTA S *et al*.: Haematological and other manifestations in the presence of antiphospholipid antibodies in a multicentric paediatric cohort. *Clin Exp Rheumatol* 2023; 41(11): 2331-37. https://doi.org/10.55563/clinexprheumatol/3mzh06
13. BALEEIRO C, DURAN CS, SIGNORELLI F, BALBI GG, BONFÁ E, ANDRADE DC: Distinct features of youth-onset primary antiphospholipid syndrome. *Lupus* 2021; 30(12): 1888-95. https://doi.org/10.1177/09612033211038054
14. ISLABÃO AG, TRINDADE VC, DA MOTA LMH, ANDRADE DCO, SILVA CA: Managing antiphospholipid syndrome in children and adolescents: current and future prospects. *Paediatr Drugs* 2022; 24(1): 13-27. https://doi.org/10.1007/s40272-021-00484-w
15. DABIT JY, VALENZUELA-ALMADA MO, VALLEGO-RAMOS S, DUARTE-GARCÍA: Epidemiology of antiphospholipid syndrome in the general population. *Curr Rheumatol Rep* 2022; 23(12). https://doi.org/10.1007/s11926-021-01038-2
16. GRIMAUD F, YELNIK C, PINETON DE CHAMBRUN *et al*.: Clinical and immunological features of antiphospholipid syndrome in the elderly: a retrospective national multicentre study. *Rheumatology* (Oxford) 2019; 58(6): 1006-10. https://doi.org/10.1093/rheumatology/key437
17. MASSON C, AN NGUYEN TT, DUFROST V *et al*.: Antiphospholipid syndrome in patients over 65 years: A comparative study of clinical and biological features and thrombotic relapses. *Lupus* 2022. 31(14): 1816-23. https://doi.org/10.1177/09612033221130975
18. ANATOLI A, BOTT C, KITTERER D *et al*.: Primary antiphospholipid syndrome in the elderly: Four strokes and mechanical thrombectomies until the diagnosis – A case report. *Brain Circ* 2024; 10(2): 184-87. https://doi.org/10.4103/bc.bc_67_23
19. DELGADO MG, RODRÍGUEZ S, GARCÍA R, SÁNCHEZ P, SÁIZ A, CALLEJA S: Antiphospholipid syndrome of late onset: a difficult diagnosis of a recurrent embolic stroke. *J Stroke Cerebrovasc Dis* 2015; 24(8): 209-11. https://doi.org/10.1016/j.jstrokecerebrovasdis.2015.04.016