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Clinical and Immunologic Profile of Women with Recurrent Pregnancy Losses in the Philippine General Hospital: A Retrospective Study from 2010-2015

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ABSTRACT

Background: Recurrent pregnancy loss (RPL) affects 1-5% of women with most cases due to autoimmune causes and around 40-50% are idiopathic. Commonly associated with RPL is antiphospholipid syndrome (APS). Investigations have revealed that several patients present only with pregnancy morbidities alongside antiphospholipid antibodies (aPL). In the Philippines, the Philippine Obstetrical and Gynecological Society has released its practice guidelines on RPL; however, local studies on RPL have been lacking.

Methodology: A retrospective review was performed on both in-patient and out-patient medical records relating to the patients' pregnancies. Patients included were those referred to the Allergy and Immunology service for suspicion of APS, aPL positivity, or history of pregnancy loss during the period of January 2010 to August 2015 with at least 2 previous spontaneous pregnancy losses and with at least one work-up for aPL.

Results: We reviewed the clinical features and immunologic profile of 78 patients with a history of at least two pregnancy losses from 2010 to 2015 followed up at our institution. The mean age of patients was 32.24 ± 5.52 years (range: 20 to 43; median: 34). There was a total of 263 previous pregnancies among the patients, 181 (68.82%) of which were abortions and 43 (16.35%) were preterm deliveries. Comorbidities present in these patients were hypertension (15), diabetes mellitus (DM) (11), asthma (6), Polycystic ovary syndrome (5), and systemic lupus erythematosus (2). Repeat test determination was only done in 18 patients; only three patients fulfilled the Sydney criteria, two in category I, and one in category IIa. Among those with single determination for aPL, 35 were reactive for LAC, 10 for aCL, and 1 for anti-β2GPI. Clinical features were not significantly associated with any obstetric complication. Single positivity of any of the aPLs was not associated with any obstetric complication.

Conclusion: This study shows a high incidence of aPL positivity among RPL patients. Although clinical factors such as hypertension and prior late pregnancy losses appeared to have an association with poor obstetric outcomes, these were not significant. Positivity to any of the aPLs also did not have a significant association with obstetric outcomes. Although largely discussed in this study is the connection of RPL and APS, several other unexplained factors of RPL could be involved in the study population.

Keywords: recurrent pregnancy loss, antiphospolipid antibody syndrome, antiphospholipid antibodies

BACKGROUND AND SIGNIFICANCE

In previous years, recurrent pregnancy loss (RPL) has been inconsistently defined. Recently however, RPL is defined by the American Society for Reproductive Medicine as two or more failed clinical pregnancies distinct from infertility.[1] RPL affects approximately 1-5% of women.[2] Investigations into RPL have found several etiologic factors, such as anatomic factors (10-15%), autoimmune (20%), endocrine factors (17-20%), genetic factors (2-5%), and infections (0.5-5%). Despite these, as much as 40-50% of RPL cases would remain unexplained.[3] In our setting, it is common practice to work patients up for antiphospholipid syndrome (APS) when they have a history of recurrent pregnancy losses.

APS has had a particular focus with regard to research on RPL due to its clear association with obstetric complications and pregnancy losses.[4] In the latest report by the International Congress on Antiphospholipid Antibodies, in a review of 46 articles, they found a positive association of antiphospholipid antibodies (aPL) with recurrent early miscarriage (<10 weeks gestation) in the majority of these studies.[5] In addition, a systematic review by Abou-Nassar et al. has shown associations between aPL with both stillbirths (>20 weeks gestation) and late fetal losses (>10 weeks gestation).[6]

Classically APS is defined as an autoimmune condition with the presence of aPLs associated with vascular thrombosis (arterial or vascular) and/or pregnancy morbidities.[4] Despite APS being a single disease, recent studies have observed differences between vascular and obstetric APS (OAPS).[7] Despite the similarity in thrombosis as the underlying mechanism of both vascular and obstetric APS, OAPS is related to several other mechanisms different from those seen in thrombotic APS, such as local inflammatory factors and complement activation.[7,8]

This has led to further investigations into cases presenting only with pregnancy morbidities. Obstetric APS is defined by Alijotas-Reig et al. as the syndrome wherein inflammation and/or thrombosis owing to aPL occur in the placenta without previous systemic thrombosis and is associated with poor obstetrical outcomes.[9] In several studies, poor obstetrical outcomes have been found to be associated with previous thrombosis, late losses as compared to early losses, and high-titer as compared to low-titer aPL.[10–13] Among the aPLs, Lupus Anticoagulant (LAC) positivity and triple positivity were found to be associated with thrombosis and poor obstetric outcomes.[14,15]

However, in the study by Bouvier and colleagues, they observed that findings in these previous studies may have been confounded by the fact that these patients also had previous thrombosis.[11] In their study looking into purely obstetric APS, aCL-M was identified as a risk factor for placenta-mediated complications, whereas LA was only associated with SGA neonates.[11] Lockshin et al. argue that LAC is the primary predictor for adverse outcomes in pregnancy after 12 weeks.[16] In their observation, despite positivity with the other aPL, if LAC is absent, these aPL will not predict adverse pregnancy outcomes. Exact contributions by specific aPL positivity to adverse pregnancy outcomes still need further investigation at this point.

Furthermore, the European Registry on Obstetric APS (EUROAPS) notes that not all women would be able to fulfill the criteria for APS (Table 1) despite suffering from known aPL-related obstetrical complications. For these cases, they were classified as "Obstetric Morbidity associated with Antiphospholipid antibody Syndrome" (OMAPS).[9] Moreover, in clinical practice in resource-limited settings, several patients would not fulfill the laboratory criteria because repeat determination would be difficult financially. Hence, patients with only 1 set of aPL tests done with obstetric complications related to aPL could be classified as OMAPS.

Locally, the Philippine Obstetrical and Gynecological Society has released its practice guidelines on RPL.[17] However, local studies regarding RPL or APS have been limited. To our knowledge, only one retrospective study was done on APS.[18] Therefore, this study aimed to investigate the clinical and immunologic profile of patients with recurrent pregnancy losses in the Philippines.

METHODOLOGY

Study Population

Patients included in this study were selected from those referred to our clinic for suspicion of APS, aPL positivity, or history of pregnancy loss during the period of January 2010 – August 2015. Inclusion criteria were: Pregnant women older than 18 years old with at least two previous spontaneous pregnancy losses; with work-up for aPL of any level done at least once: (a) LAC: Diluted Russell Viper Venom Time (DRVVT) or Kaolin Clotting Time (KCT) or Silica Clotting Time (SCT), activated Partial Thromboplastin Time (aPTT); (b) Anticardiolipin antibody (ACA) IgG or ACA IgM; (c) anti-Beta2 Glycoprotein-I antibody (anti-β_2GPI). Pregnant patients with systemic lupus erythematosus (SLE) or other thrombophilias were included. Exclusion criteria were: pregnancy losses explainable by other factors such as infectious, anatomic, hormonal, or maternal/paternal chromosomal causes; women with infertility; women who underwent artificial/assisted reproductive procedures.

Data Collection

Both in-patient and out-patient medical records relating to the patients' pregnancies from January 2010 – August 2015

Table 1. Classification Criteria for APS

Clinical Criteria Antiphospholipid antibody syndrome (APS) is present if at least one of the clinical criteria and one of the laboratory criteria that follow are met*
Vascular Thrombosis[a] One or more clinical episodes[b] of arterial, venous, or small vessel thrombosis[c], in any tissue or organ. Thrombosis must be confirmed by objective validated criteria (i.e., unequivocal findings of appropriate imaging studies or histopathology). For histopathologic confirmation, thrombosis should be present without significant evidence of inflammation in the vessel wall.
Pregnancy Morbidity Criteria 1) One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal fetal morphology documented by ultrasound or by direct examination of the fetus, or 2) One or more premature births of a morphologically normal neonate before the 34th week of gestation because of: i) eclampsia or severe preeclampsia defined according to standard definitions, or ii) recognized features of placental insufficiency[d], or 3) Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded.
Laboratory Criteria[e] 1) Lupus anticoagulant (LA) present in plasma, on two or more occasions at least 12 weeks apart, detected according to the guidelines of the International Society on Thrombosis and Haemostasis (Scientific Subcommittee on LAs/phospholipid-dependent antibodies). 2) Anticardiolipin (aCL) antibody of IgG and/or IgM isotype in serum or plasma, present in medium or high titer (i.e., >40 GPL or MPL, or >the 99th percentile), on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA. 3) Anti-B_2 glycoprotein-I antibody of IgG and/or IgM isotype in serum or plasma (in titer >the 99th percentile), present on two or more occasions, at least 12 weeks apart, measured by a standardized ELISA, according to recommended procedures.

**Classification of APS should be avoided if less than 12 weeks or more than five years separate the positive aPL test and the clinical manifestation.*

[a] Coexisting inherited or acquired factors for thrombosis are not reasons for excluding patients from APS trials. However, two subgroups of APS patients should be recognized according to: (a) the presence, and (b) the absence of additional risk factors for thrombosis. Indicative (but not exhaustive) such cases include: age (>55 in men and >65 in women), and the presence of any of the established risk factors for cardiovascular disease (hypertension, diabetes mellitus (DM), elevated LDL or low HDL cholesterol, cigarette smoking, family history of premature cardiovascular disease, body mass index ≥30 kg m^{-2}, microalbuminuria, estimated GFR <60 mL min^{-1}), inherited thrombophilias, oral contraceptives, nephrotic syndrome, malignancy, immobilization, and surgery. Thus, patients who fulfill the criteria should be stratified according to contributing causes of thrombosis.

[b] A thrombotic episode in the past could be considered as a clinical criterion, provided that thrombosis is proved by appropriate diagnostic means and that no alternative diagnosis or cause of thrombosis is found.

[c] Superficial venous thrombosis is not included in the clinical criteria.

[d] Generally accepted features of placental insufficiency include: 1) abnormal or non-reassuring fetal surveillance test(s), e.g., a non-reactive non-stress test, suggestive of fetal hypoxemia, 2) abnormal Doppler flow velocimetry waveform analysis suggestive of fetal hypoxemia, e.g., absent end-diastolic flow in the umbilical artery, 3) oligohydramnios, e.g., an amniotic fluid index of 5 cm or less, or 4) a postnatal birth weight less than the 10th percentile for the gestational age.

[e] Investigators are strongly advised to classify APS patients in studies into one of the following categories: I: More than one laboratory criteria present (any combination). IIa: Anti-cardiolipin antibody present alone. IIb: Lupus Anticoagulant present alone. IIc: Anti-b2 glycoprotein-I antibody present alone.

were reviewed. The study protocol was approved by the hospital ethics review board. We collected the following data: age, previous obstetric history (number of abortions, preterm deliveries, term deliveries), presence of co-morbid conditions (such as hypertension, diabetes mellitus (DM), SLE, history of thrombosis), history of previous obstetric complications, pregnancy outcomes (gestational age, fetal weight, maternal obstetric complications).

Results of immunologic work-up for LAC (DRVVT, SCT, KCT, aPTT), ACA (IgG and IgM), and anti-β_2GPI (IgG and IgM) were recorded. Cut-off values for medium/high titers for ACA and anti-β_2GPI were based on lab-determined 99th percentiles. Repeat aPL determination results were also recorded.

Anti-Nucleolar Antibody (ANA), Anti-double stranded DNA (Anti-dsDNA), Anti-Ro, Anti-La, Anti-thyroid peroxidase (Anti-TPO), Anti-thyroglobulin (Anti-TG), and other immunologic tests such as Lymphocyte Antibody Test (LAT) and NK cell enumeration were recorded if they were done.

Statistical Analysis

Values were expressed as mean, standard deviation, and extreme values (minimum and maximum) for continuous variables, numbers, and percentages for qualitative variables. A chi-squared test and Fisher exact test were used to compare categorical variables. Statistical analysis was done using openepi.com.

RESULTS

We were able to identify 198 patients referred to our clinic for the management of recurrent pregnancy loss or suspicion of APS. In 88 of these cases, their records were not retrieved. Fifteen were excluded for not meeting the inclusion criteria, and an additional 16 were excluded for lack of laboratory work-up or irretrievable lab results. We reviewed the clinical features and immunologic profiles of 78 patients with a history of recurrent pregnancy losses from 2010 to 2015. Of these, only 64 had complete records of their pregnancy outcomes.

The mean age of the patients was 32.24± 5.52 years (range: 20 to 43; median: 34). There was a total of 263 previous pregnancies among the patients, 181 (68.82%) of which were abortions and 43 (16.35%) were preterm deliveries (Table 2). Two-thirds of the patients (n=52) have not had a live birth. Among the 26 with live births, 8 had live births prior to the consecutive pregnancy losses, 10 had live births in between pregnancy losses, and eight did not have records. Comorbidities present in these patients were: hypertension (15), diabetes mellitus (11), asthma (6), polycystic ovary syndrome (5), and systemic lupus erythematosus (2).

Repeat test determination of aPL was done in only 18(23%) patients; only 3 patients fulfilled the Sydney criteria, 2 in category I, and 1 in category IIa. Among those with single determination or single positivity for aPL, 2 patients had positivity in 2 aPL, 35 were reactive for LAC, 10 for aCL, and 1 for anti-β_2GPI (Table 3). Other immunologic tests done were the following: anti-thyroglobulin (1), Protein C and S (1), and lymphocyte antibody test (2).

Out of 64 patients, 60 were treated with aspirin (ASA), 49 with unfractionated heparin (UFH), 7 with low-molecular-weight heparin (LWMH), and 17 with oral corticosteroids. There was incomplete data as to whether ASA was given in 4 patients, UFH in 2 patients, LMWH in 2, and prednisone in 4 patients. Pregnancy outcomes in these patients treated were as follows: 40 term deliveries (62.5%), 14 preterm deliveries (7 severe preterms, or <34 weeks AOG), 5 stillbirths, and 5 abortions. Preeclampsia was observed in 10 patients, and HELLP syndrome in only 2 patients.

Tables 4 and 5 show the association of clinical factors and aPL positivity with pregnancy morbidities. Briefly, none of the clinical factors: age, hypertension, DM, RPL classification – primary versus secondary, or timing of previous miscarriages – early (<10 weeks of gestation) versus late (≥10 weeks of gestation) were associated with any of the pregnancy morbidities. Since only a few patients fit the strict APS criteria, we analyzed aPL positivity instead. Positivity with any aPL was not associated significantly with any of the pregnancy morbidities as well. However, the lack of DRVVT positivity was associated with pregnancy complications.

Table 2. Patient Characteristics

Age (years) mean ± SD	32.25 ± 5.49 (range: 20-43)
	n (%)
Co-morbidities	29 (37.18)
Hypertension	15 (19.23)
Diabetes Mellitus	11 (13.92)
Asthma	6 (7.59)
PCOS	5 (6.33)
Previous arterial thrombosis	1 (1.27)
Heart disease	1 (1.27)
Hepatitis B	2 (2.53)
SLE	2 (2.53)
Previous Obstetric Outcomes	
Total number of pregnancies	264
Recurrent abortion	69 (87.34)
Preterm delivery	25 (31.65)
>1 Preterm delivery	13 (16.46)
Fetal Death in Utero	9 (3.40)
Without any live children	53 (67.09)
Total number of women with live children	26 (32.91)

Table 3. Prevalence of Antiphospholipid Antibodies

Laboratory Category / Class and Isotype of aPL	n/N	(%)
I		
Triple Positive	0	0
Double Positive	**2/18**	11.11
LA+ aCL IgG+ IgM-	1/18	5.56
LA+ aCL IgG- IgM+	1/18	5.56
II		
IIa		
Lupus anticoagulant	**1/18**	5.56
Single Determination Positivity		
Triple Positivity	0	0
Double Positivity		
LA+ aCL IgG+ IgM-	**2/76**	2.63
Lupus anticoagulant	**35/74**	47.30
DRVVT	20/70	28.57
SCT	16/56	28.57
KCT	8/19	42.11
aPTT	7/68	10.29
Anticardiolipin Antibody	**10/60**	16.67
ACA IgG	1/60	1.67
ACA IgM	9/60	15.00
Anti-β_2GPI antibodies	**1/9**	11.11
Anti-β_2GPI IgM isotype	1/9	11.11

DISCUSSION

In this study, we analyzed important clinical and immunologic features of women with recurrent pregnancy losses. As with any retrospective study, data regarding other work-up may be lacking or incomplete. Most investigations into RPL in our study found that clinicians primarily focused on antiphospholipid antibodies. Other causes of recurrent pregnancy loss – thrombophilia, autoimmunity, autoimmune thyroiditis, were not explored. It would be good to note that around 40% of patients with RPL may be due to unexplained factors.[3] Most investigations were not able to do repeat determinations due to budget constraints, among other undetermined factors.

Clinical Factors

Our study found no significant association between clinical factors and obstetric complications. The presence of

hypertension had more complications (58.33% vs. 38.46%), as well as preterm deliveries (50% vs. 19.05%), SGA neonates (41.67% vs. 19.05%), and preeclampsia (33.33% vs. 11.54%). Late miscarriages had more complications than those who had early miscarriages (46.34% vs. 35.71%) and had more preterm deliveries (33.33% vs. 16.67%) and SGA neonates (24.24% vs. 8.33%). However, all these observations did not reach statistical significance. These findings are congruent with findings in Bouvier's study and those in other prior reports.[11]

Antiphospholipid Antibodies

Previous studies have estimated the incidence of aPL in women with RPL to be at 20-40%, whereas in women with a normal obstetric history, it is only 3%.[19] Therefore, APS is possibly one of the leading causes of RPL. However, a

Table 4. Clinical profile and pregnancy morbidities

	Any Complication n (%)	Preterm Delivery n (%)	SGA n (%)	Abortion n (%)	Stillbirth n (%)	Preeclampsia n (%)	HELLP n (%)
Age							
20-29 (n=22)	8 (36.36)	4 (22.22)	4 (22.22)	1 (4.55)	3 (13.64)	5 (22.73)	2 (9.09)
30-39 (n=37)	18 (48.65)	9 (29.03)	8 (25.81)	4 (10.81)	2 (5.41)	5 (13.51)	0
40+ (n=5)	1 (20)	1 (20)	1 (20)	0	0	0	0
Hypertension							
Positive (n=12)	7 (58.33)	6 (50)	5 (41.67)	0	0	4 (33.33)	1 (8.33)
Negative (n=52)	20 (38.46)	8 (19.05)	8 (19.05)	5 (9.62)	5 (9.62)	6 (11.54)	1 (1.92)
Diabetes Mellitus							
Positive (n=10)	5 (50)	4 (40)	3 (30)	0	0	1 (10)	0
Negative (n=54)	22 (40.74)	10 (22.73)	10 (22.73)	5 (9.26)	5 (9.26)	9 (16.67)	2 (3.7)
RPL Classification							
Primary (n=52)	23 (44.23)	12 (27.27)	12 (27.27)	4 (7.69)	4 (7.69)	9 (17.31)	2 (3.85)
Secondary (n=10)	4 (40)	2 (25)	1 (12.5)	1 (10)	1 (10)	1 (10)	0
Previous Miscarriages							
Early (<10wks) (n=14)	5 (35.71)	2 (16.67)	1 (8.33)	1 (7.14)	1 (7.14)	2 (14.29)	1 (7.14)
Late (≥10wks) (n=41)	19 (46.34)	11 (33.33)	8 (24.24)	4 (9.76)	4 (9.76)	7 (17.07)	1 (2.44)

Table 5. Antiphospholipid antibody positivity and pregnancy morbidities

	Any Complication n (%)	Preterm Delivery n (%)	SGA n (%)	Abortion n (%)	Stillbirth n (%)	Preeclampsia n (%)	HELLP n (%)
aPL Test Positivity							
Positive (n=40)	16 (40)	8 (24.24)	6 (18.18)	4 (10)	3 (7.50)	6 (15)	2 (5)
Negative (n=24)	11 (45.83)	6 (28.57)	7 (33.33)	1 (4)	2 (8.33)	4 (16)	0
ACA							
Positive (n=10)	3 (30)	2 (22.22)	2 (22.22)	1 (10)	0	2 (20)	1 (10)
Negative (n=41)	20 (48.78)	9 (27.27)	8 (24.24)	3 (7.14)	5 (12.2)	6 (14.29)	1 (2.38)
LAC							
Positive (n=31)	14 (45.16)	7 (28)	5 (20)	3 (9.68)	3 (9.68)	5 (16.13)	2 (6.45)
Negative (n=32)	13 (40.62)	7 (25)	8 (28.57)	2 (6.06)	2 (6.25)	5 (15.15)	0
DRVVT							
Positive (n=18)	**4 (22.22)***	3 (17.65)	1 (5.88)	0	1 (5.56)	3 (16.67)	2 (11.11)
Negative (n=41)	**21 (51.22)**	9 (28.12)	10 (31.25)	5 (11.9)	4 (9.76)	6 (14.29)	0
SCT							
Positive (n=16)	10 (62.5)	5 (45.45)	4 (36.36)	3 (18.75)	2 (12.5)	3 (18.75)	1 (6.25)
Negative (n=33)	12 (36.36)	6 (20)	7 (23.33)	1 (2.94)	2 (6.06)	4 (11.76)	1 (2.94)
KCT							
Positive (n=4)	1 (25)	1 (25)	0	0	0	0	0
Negative (n=11)	4 (36.36)	2 (22.22)	1 (11.11)	1 (9.09)	1 (9.09)	1 (9.09)	0
aPTT							
Positive (n=9)	3 (33.33)	1 (12.5)	2 (25)	1 (11.11)	0	1 (11.11)	1 (11.11)
Negative (n=50)	21 (42)	11 (16.83)	8 (19.51)	4 (7.84)	5 (10)	8 (15.69)	1 (1.96)
Anti-β_2GPI							
Positive (n=2)	2 (100)	1 (100)	1 (100)	1 (50)	0	1 (50)	1 (50)
Negative (n=7)	4 (57.14)	2 (40)	2 (40)	1 (14.29)	1 (14.29)	0	0

** <0.05*

few other studies have estimated the incidence of aPL positivity to be much lower at 2.7% to 17.4%.[20,21] In our study, we observed aPL positivity in 61.5%. In particular, LACs were the most prevalent among the aPL (47.3%). As in the Task Force report by de Jesus et al., several studies have indeed found a high prevalence of aPL in patients with REM.[5] A high prevalence of aPL in our study could be explained by the lack of repeat aPL test determination in a majority of our population. Some positive aPL cases could be transient elevations only. Transient positivity of aPL, as noted by Abou-Nassar et al., is of uncertain significance and may contribute to heterogeneity in observed populations.[6] Nonetheless, findings support the role of aPL in RPL in our population.

With regard to the association of DRVVT negativity and obstetric complication, we cannot explain this finding adequately. It is entirely possible that cases were confounded with low-titer levels and that these were classified as negative DRVVT. Furthermore, the LAC tests taken singly may not lead to proper conclusions and morbidity associations.

Studies conducted on women with RPL and APS have found an association between triple aPL positivity and poor obstetric outcomes.[10] In our study, we were not able to find any significant association between aPL positivity and obstetric complications. This may have been brought about by having a heterogenous population. Studies looking into associations of aPL positivity and obstetric outcomes included only those having early abortions, while our study included those having early and late miscarriages. The limitation of not being able to repeat aPL determination could also be a contributing factor. Some cases may not have had persistent elevations of aPL titers.

Results regarding aPL association with obstetric complications are inconclusive at this point. Only three patients fit the criteria set about in the international consensus on APS. A large majority of patients did not fit the criteria or failed to have a repeat determination of aPL positivity.

However, several authors have argued that OAPS has a different manifestation compared to patients with classic APS. This was initially observed in the study by Cervera et al., wherein they found that most cases of OAPS did not have manifestations of thrombosis.[22] The majority of our study population did not have a prior history of thrombosis and only had obstetric complications. Only one patient had a previous history of thrombosis.

Patients with OAPS also have a different aPL titer compared to classic APS. In a recent study by Mayer-Pickel, they observed a higher prevalence of triple positivity in OAPS and there was a higher prevalence of LAC positivity in thrombotic APS.[23] In several large studies, majority of women with RPL only had low levels of aPL or would only be detected transiently.[21,24,25] Furthermore, regardless of aPL positivity and independent of treatment, studies have found good prognoses for women with RPL in their subsequent pregnancy.[25,26] Contrary to this, a study by Mekinian et al showed that if women with OAP of low aPL titers were left untreated, they would have similar poor pregnancy outcomes as women with the classic APS.[27] When treated however with ASA ± LMWH, they observed improvement in these outcomes approximating that of RPL from unexplained factors. Moreover, from the preliminary results of EUROAPS, regardless of being able to fulfill the strict criteria for APS – be it the clinical or laboratory criteria, pregnancy outcomes in women with OAPS and OMAPS treated with ASA or LMWH or both did not differ significantly (79.4% and 93.7% respectively).[9]

CONCLUSION

In conclusion, this study has identified the prevalence and characteristics of important clinical and immunologic features of women with RPL in the Philippines. From this retrospective analysis, we were able to observe a high incidence of aPL positivity among RPL patients. Although clinical factors such as hypertension and prior late pregnancy losses appeared to have an association with poor obstetric outcomes, these were not significant. None of the aPLs had a significant association with any of the obstetric morbidities.

There was also a low percentage of patients who were able to undergo repeat determinations of aPL and this was one of the limitations of our study. Low titer aPL was no longer explored in this study, but as seen from previous reports, this merits further investigation. It is entirely possible that OAPS can have a risk stratification with high- and low-titer aPL.

This study has also only explored the connection between RPL and APS. However, as mentioned earlier, several other factors still weigh in on RPL. A large percentage of RPLs are due to unexplained factors. It is important to note that other investigations could benefit patients with RPL, particularly those with negative aPL.

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