Original Research Article

Role of Antiphoso lipid anti-bodies and Antinuclear anti-bodies in pregnancy outcome and its treatment for better outcome

Alka Dani[1], Abhishek[2*]

[1]Associate Professor, [2]Assistant Professor, Department of OBGY, Dr. D.Y.Patil Medical College, Hospital and Research Centre, Nerul, Navi Mumbai INDIA.
Email: alka.dani@gmail.com

Abstract

Background: Patients with raised titre of ANA antibodies and APLA during pregnancy have more guarded prognosis like recurrent pregnancy loss, preterm delivery, lUGR, oligohydramnios, stillbirth and maternal complications like severe rhehmatoid arthritis, SLE,lTP, rashes, multiorgan failure in cases of positive ANA test and severe preeclampsia, venous and arterial thrombosis, stroke, coronary artery thrombosis if APLA is positive. **Aims and objectives**: In this study our objectives are to assess the role of ANA and APLA on maternal and fetal health and to diagnose and treat the condition early in pregnancy to improve the outcomes. **Material and Methods:** In this study 55 cases with h/o RPL and adverse maternal and fetal outcome in previous pregnancies and subchorionic haemorrhage in first trimester during current pregnancy were studied for presence of ANA, LAC and ACLA and their titers and serial sonography was done. Patient's councelling and treatment started accordingly and test was repeated after 12weeks and maternal and fetal outcome was noted and analysed. Result- Out of 55patients 63.6% were ANA+ positive and 29.1% were ANA2+ positive. ACLA was positive in 12.7% and LAC in 3.3% of patients. 38.2% of patients had PIH, 20% GDM, 20% hypothyroidism and12.7% patients had hyperthyroidism. In 63.6% patients, USG findings were abnormal. 78.2% patients had good fetal outcome while 21=8% patients had poor fetal outcome. **Conclusion:** ANA and APLA test should not be done as a routine but only in risk cases for early detection and prompt treatment so as to improve pregnancy course and fetal outcome.
Keywords: Recurrent pregnancy loss, Antinuclear antibodies, Antiphospholipid antibodies.

[*]**Address for Correspondence:**
Dr Abhishek, Assistant Professor, Department of OBGY, Dr. D.Y.Patil Medical College, Hospital and Research Centre, Nerul, Navi Mumbai INDIA.
Email: alka.dani@gmail.com
Received Date: 02/12/2019 Revised Date: 08/01/2020 Accepted Date: 11/02/2020
DOI: https://doi.org/10.26611/10121331

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 03 March 2020

INTRODUCTION

Patients who have raisedtitre of antinuclear anti-bodies (ANA) and antiphosolipid anti-bodies(APLA) during pregnancy have a more guarded prognosis like recurrent miscarriage, pre-term delivery, intra-uterine growth retardation (IUGR), oligohydramnios, still birth and maternal complications like severe rheumatoid arthritis, SLE, auto immune thrombocytopenia, rashes and multi-organ failure in case of positive ANA test and severe pre-eclampsia, venous and arterial thrombosis, stroke, coronary artery thrombosis if APLA is positive. APLA includes lupus anticoagulant (LAC) AB and anticardolipin (ACL) AB. Incidence of LAC in India is 15-30% and ACL is 23-86%. These patients are more likely to get benefitted by therapeutic interventions like Aspirin, Heparin and Prednisolone. The ANA Test was designed by Dr. George Friou in 1957. It can also refer to as fluorescent antinuclear anti-body test (FANA). It is a sensitive screening test used to detect autoimmune diseases. ANA can be found in approximately 5% of normal population in low titers. ANA titer of <= 1:40 are considered negative. Those with higher titers have been found to have a risk of RPL and are more

How to cite this article: Alka Dani, Abhishek. Role of Antiphoso lipid anti-bodies and Antinuclear anti-bodies in pregnancy outcome and its treatment for better outcome. *MedPulse International Journal of Gynaecology.* March 2020; 13(3): 75-80.
http://medpulse.in/Gynacology/index.php

likely to be benefitted from Prednisone. In 1983 Hughes first described patients with the combination of clinical features (i.e. thrombosis, thrombocytopenia, RPL, IUGR, pre-eclampsia) associated with the presence of APLA and LAC. Primary method of diagnosis requires clinical and laboratory findings with the clinical criteria and should be tested for both LAC and ACL immunoglobulins (IgG and IgM).

Patho-physiology:

Human APLA reacts with endothelial structures[1] which disturbs the PGE_2/Thromboxane production balance[2], interaction with platelet PLs with consequent upregulation of platelet aggregation[3], dysregulation of compliment activation and[4] interaction of APL with phosphatidyl serine expose during trophoblast syncytium formation resulting in more direct effect of APLA on placental structure.

APS is associated with increased maternal morbidity and mortality as well as increased perinatal MMR. It is associated with increased risk of venous and arterial thrombosis, coronary artery occlusion. There is increased incidence of pre-eclampsia usually before 34 weeks, pre-mature deliveries, infertility, spontaneous abortion and still births. MOFD has been described during pregnancies by Asherson[1] and during puerperium by Kochenom.[2] Neonatal morbidity and mortality is due to severe pre-eclampsia and IUGR. Rate of fetal loss can be reduced by 20% by therapy (Aspirin and Heparin) as described by Cowchok *et al*[3].

Aims and Objectives

To assess the role of Antinuclear antibody and Antiphospholipid antibody on maternal and fetal health. To diagnose and treat the condition early in pregnancy to improve outcomes. To study relation of relative titers of ANA with other anti-bodies and with adverse pregnancy outcomes.

MATERIAL AND METHODS

This prospective case study was conducted in a tertiary hospital of Mumbai from February 2009 to April 2011. Ethical committee approval was taken. After taking informed written consent, 50 cases with history of RPL and adverse maternal and fetal outcome in previous pregnancies like pre-term birth, IUGR, miscarriage, still births, IUFD, severe PIH in second trimester, subchorionic haemorrhage in first trimester during current pregnancy were included in the study and those with history of MTP, chronic hypertension without pregnancy losses and with normal pregnancy course were excluded from the study. Routine anti-natal and special investigations (ANA, LAC, ACLA) were done along with serial sonography. After the test results patient's counselling was done for probability of adverse pregnancy course (PIH, GDM and Thyroid dysfunction) and increased risk of adverse fetal outcome (missed abortion, pre-term labour, oligohydramnios, IUFD, IUGR). Patients with positive ANA, ACLA, LAC were then referred to the hospital rheumatologist for treatment and other immunological disorders. Then tests were repeated after 12 weeks and patients were also treated for PIH, GDM and thyroid dysfunction if present. USG was done in first trimester to detect subchorionichaemorrhage, missed abortion, blighted ovum and for nuchal translucency along with double marker test to rule out chromosomal anomalies. Second trimester anomalies scan and triple marker test was done between 18-20 weeks. GCT was done between 24-26 weeks. GTT was done if GCT was abnormal to detect GDM. Weight and BP were checked during each antenatal visit. During third trimester, along with routine checkup colour doppler studies were done on USG every 3-4 weeks to check fetal growth. Patients were asked to keep strict daily fetal movements count. Low dose of Aspirin was given to treat patients with increased APLA and ANA titers. Prednisolone and Hydroxychloroquine were also given to patient with autoimmune disorders. Aspirin and Prednisolone were stopped at 36 weeks of gestation. All the information was filled in the predesigned Performa. Data analysis was done using software SPSS for windows v.15.0

RESULTS

Table 1: Descriptive Statistics of Demographic Variables

Variables	N	Mean	Stdev	Median	IQR
Age(yrs)	55	29.6727	5.4128	29	8
Married(yrs)	55	4.4545	3.0901	4	5
Gravida	55	2.1818	1.4154	2	2
Parity	55	0.5636	0.7641	0	1
Abortion	55	0.6727	1.0193	0	1
Live Births	55	0.4000	0.7354	0	1

Table 2: Distribution of study group as per history of Hypertension

HTN	No. of Females	Percentage
PIH	21	38.2
No	34	61.8
Total	**55**	**100.0**

Table 3: Distribution of study group as per history of Diabetes

Diabetes MOD	No. of Females	Percentage
GDM	11	20.0
No	44	80.0
Total	**55**	**100.0**

Table 4: Distribution of study group as per Thyroid function test

Thyroid function test	No. of Females	Percentage
Hypothyroidism	11	20.0
Hyperthyroidism	7	12.7
No	37	67.3
Total	**55**	**100.0**

Table 5: Distribution of study group as per result of ANA

ANA	No. of Females	Percentage
1+	35	63.6
2+	16	29.1
No	4	7.3
Total	**55**	**100.0**

Table 6: Distribution of study group as per result of ACL

ACL	No. of Females	Percentage
Positive	7	12.7
Negative	48	87.3
Total	**55**	**100.0**

Table 7: Distribution of study group as per result of AL

ACL	No. of Females	Percentage
Positive	2	3.6
Negative	53	96.4
Total	**55**	**100.0**

Table No 8: Distribution of study group as per USG finding

USG	No. of Females	Percentage
Normal	20	36.4
Abnormal	35	63.6
Total	**55**	**100.0**

Table No 9: Distribution of study group as per history of Treatment taken

Treatment taken	No. of Females	Percentage
Yes	39	70.9
No	16	29.1
Total	**55**	**100.0**

Table 10: Distribution of study group as per outcome of pregnancy

Outcome	No. of Females	Percentage
Good	43	78.2
Bad	12	21.8
Total	55	100.0

Table 11: Distribution of study group as per IUFD

IUFD	No. of Females	Percentage
Yes	7	12.7
No	48	87.3
Total	**55**	**100.0**

Table 12: Association ANA variable with other Parameters

Parameters	ANA				Chi square Test	P-Value	Significant at 5% Level
HTN	1+	2+	Negative	Total			
PIH	14	6	1	21	0.347	0.841	No
No	21	10	3	34			
Total	35	16	4	55			
Diabetes MOD							
GDM	7	2	2	11	2.813	0.245	No
No	28	14	2	44			
Total	35	16	4	55			
Thyroid function test							
Hypothyroidism	4	7	0	11	9.383	0.052	No
Hyperthyroidism	5	2	0	7			
No	26	7	4	37			
Total	35	16	4	55			
ACL							
Negative	32	14	2	48	5.548	0.062	No
Positive	3	2	2	7			
Total	35	16	4	55			
USG							
Abnormal	20	13	2	35	3.104	0.212	No
Normal	15	3	2	20			
Total	35	16	4	55			
Treatment taken							
Yes	27	11	1	39	4.782	0.092	No
No	8	5	3	16			
Total	35	16	4	55			
LA							
Negative	34	15	4	53	0.524	0.770	No
Positive	1	1	0	2			
Total	35	16	4	55			

Outcome							
Good	28	11	4	43	2.019	0.364	No
Bad	7	5	0	12			
Total	35	16	4	55			

Table 13: Association USG variable with other Parameters

Parameters	USG			Chi square Test	P-Value	Significant at 5% Level
	Abnormal	Normal	Total			
HTN						
PIH	14	7	21	0.135	0.714	No
No	21	13	34			
Total	35	20	55			
Diabetes MOD						
GDM	7	4	11	0.000	1.000	No
No	28	16	44			
Total	35	20	55			
Thyroid function test						
Hypothyroidism	8	3	11	0.555	0.758	No
Hyperthyroidism	4	3	7			
No	23	14	37			
Total	35	20	55			
ACL						
Negative	29	19	48	1.690	0.194	No
Positive	6	1	7			
Total	35	20	55			
Treatment taken						
Yes	22	17	39	3.025	0.082	No
No	13	3	16			
Total	35	20	55			
LA						
Negative	33	20	53	1.186	0.276	No
Positive	2	0	2			
Total	35	20	55			
Outcome						
Good	24	19	43	5.211*	0.022	Yes
Bad	11	1	12			
Total	35	20	55			

*Statistically Significant at 5% level i.e., P<0.05 .

Table 14: Association Outcome variable with other Parameters

Parameters	Outcome			Chi square Test	P-Value	Significant at 5% Level
	Bad	Good	Total			
HTN						
PIH	2	19	21	3.010	0.083	No
No	10	24	34			
Total	12	43	55			
Diabetes MOD						
GDM	1	10	11	1.306	0.253	No
No	11	33	44			
Total	12	43	55			
Thyroid function test						
Hypothyroidism	5	6	11	5.739	0.057	No
Hyperthyroidism	0	7	7			
No	7	30	37			
Total						
ACL						
Negative	10	38	48	0.214	0.643	No
Positive	2	5	7			

Total	12	43	55			
Treatment taken						
Yes	2	37	39	21.892*	<0.001	Yes
No	10	6	16			
Total	12	43	55			
LA						
Negative	12	41	53	0.579	0.447	No
Positive	0	2	2			
Total	12	43	55			

*Statistically Significant at 5% level i.e., P<0.05 .

In this study of 55 patients average age of patients was between 20_42 years with a mean of 30. Average of married life was between 1_12yr with a mean of 4.45yr. 38.2% patients had PIH, 20% patients had GDM, 20% patients had hypothyroidism, 12.7% patients had hyperthyroidism. In 63.6% patients USG findings were abnormal (IUGR, Oligohydramnios, IUFD,). ANA1+ was present in 63.6% of patients, ANA2+ was present in 29.1%,ACLA in 12.7% patients and LAC in 3.3% patients. 78.2% of patients had taken treatment and 78.2% patients had good fetal outcome while 21.8% patients had bad fetal outcome and12.7% ended up with IUFD or missed abortions. Those who were ANA 1+ or 2+ positive, 40% and 37.5% patients had PIH respectively with p value of 0.84 which is not significant statistically. 20% and 12.5% patients had GDM with ANA+ and ANA2+ respectively with p value of 0.245 (not significant) 11.42% and 43.75% patients had hypothyroidism in presence of ANA+ and ANA2+ respectively and hyperthyroidism was present in 14.2% and 12.5% of patients respectively with p value of 0.052 which is not significant statistically. Abnormal USG findings were present in 57.14% and 81.25% of patients with ANA+ and ANA 2+ positive patients respectively with p value of 0.212 (not significant). 72.14% patients with ANA+ and 68.75% patients with ANA 2+ had taken treatment. Bad fetal outcome was 20% and 31.25% in ANA+ and ANA 2+ positive patients respectively with p value of 0.364 (statistically not significant). 8 patients were APLA (ACL antibodies + LA antibodies) positive, out of which 25% had PIH, 12.5% had GDM, and 25% had hypothyroidism. It was found that 63.6% patients had abnormal USG findings, 21.8% patients had bad fetal outcome and 70.9% patients had taken treatment. It was also observed in this study that multiparae(>1 issue) and married life 5 or more years, had better prognosis. P values of these parameters is 0.018 and 0.024 respectively which is statistically significant. Bad fetal outcome in presence of PIH with APLA positive patients was16.6%, in GDM patients, 8.33%, in hypothyroidism patients 41.66%, hyperthyroidism patients 0 %, in patients with abnormal USG findings 31.42% and in those who had not taken treatment it was 83.33%. Significant impact on pregnancy outcome was associated with abnormal USG findings and treatment taken or not. P value of these parameters are 0.022 and 0.001 which is statistically significant.

DISCUSSION

Association of APLA with adverse pregnancy outcome is documented since long however association of ANA with recurrent pregnancy loss or adverse course during pregnancy is still debatable. Kutteh WH *et al* from USA in1996found that 17.3% patients with recurrent pregnancy loss(RPL) had positive ACLA, 10.1% women were positive for another APLA [5] while in our study it was 16%.Kumar KSD *et al* from India in 2002 reported importance and usefulness of screening of APLA in women experiencing RPL as a mandatory routine for instituting efficient therapeutic regimen for a successful outcome of pregnancy (6),in this study successful outcome. S Velayuthaprabhu *et al* from India in 2005 reported that levels of aCL IgG and aPS IgG were detected as 40% and 19% respectively in women with history of recurrent abortions (7). Rosalind *et al* from Pittsburgh found that previous adverse pregnancy outcome was the most important risk factor for an adverse outcome in subsequent pregnancy [8]. Luis H. *et al* in 1992 reported that efficacy of treatment with prednisolone and aspirin in cases of RPL with the antiphospholipid syndrome. They found that prior to therapy, the rate of live-born babies was 15.6% , and after therapy, it was 100%. In this study we also got 100% successful pregnancy outcome. There was no significant adverse effects on either mother or babies[9].In May 1999 J Associate Physician (authorized by Chakraborty S, Bhunia C, Bhattacharya DK,) recommended that detection of APL antibodies must be considered in women with previous pregnancies complicated by unexplained fetal wastages [10].Giasuddin *et al* from Bangladesh reported in 2010 that prevalence of ACA in patients with recurrent pregnancy loss was37.1% while in control group it was 5.4%[11].

CONCLUSION

From this progressive case study we conclude that ANA and APLA should not be done as a routine but only in risk cases and in patients with poor pregnancy outcome in

previous pregnancies as to improve pregnancy course as well as outcome.

REFERENCES

1. Asherson RA, Khamashta MA, Ordi-Ros J, Derksen RH, Machin SJ, Barquinero J, *et al*. The "primary" antiphospholipid syndrome: major clinical and serological features. *Medicine (Baltimore)*. Nov 1989;68(6):366-74.
2. Kochenour NK, Branch DW, Rote NS, *et al*. A new postpartum syndrome associated with antiphospholipid antibodies. *Obstet Gynecol*. Mar 1987; 69(3 Pt 2):460-8.
3. Cowchock FS, Reece EA, Balaban D, *et al*. Repeated fetal losses associated with antiphospholipid antibodies: a collaborative randomized trial comparing prednisone with low-dose heparin treatment. *Am J Obstet Gynecol*. May 1992;166(5):1318-23.
4. Wilson WA, Gharavi AE, Koike T, Lockshin MD, Branch DW, Piette JC, *et al*. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome: report of an international workshop. *Arthritis Rheum*. Jul 1999;42(7):1309-11.
5. Antiphospholipid antibodies (APA) and recurrent pregnancy loss: treating a unique APA positivepopulation* R.D. Franklin and W.H. Kutteh1,Hum.Reprod. (2002) 17 (11):2981,2985.doi: 10. 1093/humrep/17.11.298.
6. Kumar KSD, Jyothy A, Prakash MS, Rani HS, Reddy PP from Institute of Genetics and Hospital for Genetic Diseases, Osmania University, Begumpet, Hyderabad, India and National Institute of Nutrition, ICMR, Tarnaka, Hyderabad, India. Journal of Postgraduate Medicine, Vol. 48, Issue 1, 2002 .
7. Velayuthaprabhu S, Archunan G. Evaluation of anticardiolipin antibodies and antiphosphatidylserine antibodies in women with recurrent abortion. Indian J Med Sci. 2005 Aug; 59(8):347-52.
8. Rosalind Ramsey-Goldman[1],[2], Joan E. Kutzer[1], *et al*l Pregnancy Outcome and Anti-Cardiolipin Antibody in Women with Systemic Lupus Erythematosus, Am. J. Epidemiol. (1993) 138 (12):1057-1069.
9. Luis H. Silveira, M.D.Chris L. Hubble, *et al*l American Journal of Medicine Volume 93, Issue 4 , in October 1992 published a paper on Prevention of anticardiolipin antibody-related pregnancy losses with prednisone and aspirin.
10. Chakrabarti S, Bhunia C, Bhattacharya DK, The prevalence of antiphospholipid antibodies in cases of recurrent pregnancy loss, J Assoc Physicians India. 1999 May; 47(5):496-8.
11. Giasuddin AS, Mazhar I, Haq AM Prevalence of anticardiolipin antibody in Bangladeshi patients with recurrent pregnancy loss, Bangladesh Med Res Counc Bull. 2010 Apr;36(1):10-3.

Source of Support: None Declared
Conflict of Interest: None Declared