

International Journal of Ayurveda and Pharma Research

Review Article

CRITICAL ANALYSIS OF JATAHARINIES WSR TO ANTIPHOSPHOLIPID ANTIBODY SYNDROME

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ABSTRACT

Acharya Kashyapa in Revatikalpa adhyaya explained about the Jataharinies, as a group of demons who has divine vision, attack women to destroy or to produce serious problems of menstrual cycle, recurrent abortions, still birth, intrauterine fetal death, neonatal deaths or severe disorders which decreases the life span of the fetus. As recurrent miscarriage, intrauterine death of an infant or death at birth has always been a devastating experience for the mother and of concern in clinical practice. All these mortality remains a challenge in the care of pregnant women worldwide, particularly for those who had history of adverse outcome in previous pregnancies (BOH). Antiphospholipid antibody syndrome (Hughes syndrome) is an autoimmune, hypercoagulable state caused by antiphospholipid antibodies. Pregnancy related complications are miscarriage, still birth, preterm delivery, IUD etc. This is one of the few treatable causes of pregnancy loss, and successful pregnancy rates of 70% or more can be achieved with appropriate treatment. Description of Jataharinies resemble with APLA, hence critical analysis will help to emphasize on management of Jataharinies by Ayurvedic treatment principles.

KEYWORDS: *Jataharinies,* Anti-phospholipid antibody syndrome, BOH.

INTRODUCTION

Pregnancy is unique, exciting and joyous time in woman's life as it highlights woman's amazing creative power. Many of auto immune diseases have predisposition for woman in their child bearing age^[1]. With the exception of pregnancy with rheumatoid arthritis auto immune diseases are associated with increased risk of adverse pregnancy outcome. Antiphospholipid antibody syndrome (APLA Syndrome) is an autoimmune, hyper coagulable state caused by Antiphospholipid antibodies. Pregnancy related complications are such as miscarriage, stillbirth, Intra I.U.D (Intra uterine death) etc. It is one of the few treatable causes of pregnancy loss and successful pregnancy rates of 70% or more can be achieved with appropriate treatment.

In our classics *Kasyapa Samhita, Kalpasthanam,* chapter-6 *"Revatikalpadhyaya*" it has been mentioned that due to misdeeds of pregnant mother and father, *"Jataharinies*" kill the mother and fetus^[2]. She causes loss of progeny, loss of longevity of children due to one's own misdeeds. The *Jataharinies,* means a group of demons who have divine vision, attack women to destroy or to produce serious problems of menstrual cycle, recurrent abortions, still birth, intra uterine fetal death, neonatal deaths or severe disorders which decreases the life span of the fetus.

Incidence^[3]- It is 15-17% in European and American whites. 1-2% in India. The incidence of Rh- negativity at Safdarjung hospital is 7%. 15 percent of more than 1000 women with recurrent pregnancy loss had recognized autoimmune factors. [Kutteh and Pasquarette (1995)]. The incidence of APLA in general obstetrical population is about 5%.

Review of Jataharini

Causes and effect of Jataharinies Affliction

According to *Kasyapa Samhita* causes of *Jataharini* attack can be summarized as^[4,5,6,7]

- Adharma
- *Mithyahara-Vihara* or *Dosha Prakopaka nidanas* either male or female partners
- Susceptible stages are menstruating woman, pregnant woman, puerperal woman and the lady who lives in Hut.

These women are likely to get afflicted by *Jataharini* which can be observed by-

- 1. Destruction of Menstruation
- 2. Destruction of Fetus
- 3. Stillbirth
- 4. I.U.D

Types of *Jataharinies*^[8]- On the basis of prognosis these are of three types

- A) Sadhya (curable)
- B) Yapva (easily relapsable)
- C) Asadhya (Incurable)

A) Sadhva Jataharinies- 11 in number

- 1. Shushka revati
- 2. Katmabhara
- 3. Pushpaghni
- 4. Vikuta
- 5. Parisruta
- 6. Andaghni
- 7. Durdhara
- 8. Kalaratri
- 9. Mohini
- 10. Stambhani
- 11. Kroshana

B) Yapya Jataharinies - 16 in number

- 1. Nakini
- 2. Pishachi
- 3. Yakshi
- 4. Aasuri
- 5. Kali
- 6. Varuni
- 7. Shashti
- 8. Bhiruka
- 9. Yamva
- 10. Matangi
- 11. Bhadrakali
- 12. Raudri
- 13. Vardhika
- 14. Chandika

- 15. Kapalamalini
- 16. Pilipichchika

C) Asadhya Jataharinies- 8 in number

- 1. Vashva
- 2. Kulkshavakari
- 3. Punyajani
- 4. Paurushadini
- 5. Samdanshi
- 6. Karkotaki
- 7. Indravadava
- 8. Badvamukhi

Types of Jataharinies (on the basis of mode of transmission) according to another classification^[9]

- 3 types
- a) Daivi (devine)

Acharya Kashyapa after getting knowledge of Revati by his intense penance (Tapa) and described it to his disciples for the sake of universe.

- b) Manushi (human)- It is sub-classified into four
 - 1. Varna
 - 2. Varnantara
 - 3. Lingini
 - 4. Karuki
- c) Tirashchin (animals)- It is sub-classified into five
 - 1. Shakuni (Birds)
 - 2. Vanaspati (plants)
 - 3. Chatushpadi (four legged animals)
 - 4. Matsi (fishes)
 - 5. Sarpa (Reptiles)

Sadhya Jataharinies- In alive mothers these are 10 or 11 in number

No.	Name of Jataharinies	Properties mentioned by Kashyapa	Inference
1	Shushka revati	Girls not getting menarche at the age of 16 or lady who is emaciated having delayed menses	Delayed menarche or amenorrhoea due to nutritional or hormonal cases
2	Katambhara	The woman who is emaciated, weak, and irritable, dies in her mature age without having menstruation	Primary amenorrhoea
3	Pushpaghni	Although woman gets her menstruation at time but she has anovular menstruation so she is unable to conceive and suffers from obesity, fatty cheeks with hairs	Polycystic ovarian syndrome or excessive androgen levels
4	Vikuta	Woman gets menstruation but suffering from irregularity in duration, colour, amount and feels exhausted without any cause	Irregular menstrual and Ovulatory cycle.
5	Parisruta	Emaciated woman having constant and excessive discharge per vaginum	Excessive leucorrhoea or discharges due to infections
6	Andaghni	Causes repeated early abortions at blastocyst stage	Early abortions at Blastocyst stage

Sushma. Critical Analysis of Jataharinies wsr to Antiphospholipid Antibody Syndrome

7	Durdhara	Causes repeated abortions after formation of <i>Garbhanga</i> and harms life of woman	First and second trimester abortions
8	Kalaratri	Destroys the fetus possessing complete body suddenly, along with threat to the life of mother.	Sudden fetal death
9	Mohini	Causes non attachment of embryo or its expulsion after attachment along with death of woman.	Rupture of ectopic pregnancy or
10	Stambhani	Fetus does not quiver	Intra uterine demise
11	Kroshana	Fetus situated in uterus creates various complications	Irritable uterus i.e. threatened abortion

Yapya Jataharinies- These are sixteen in number. In woman doing righteous acts these are relapsable.

No.	Name of Jataharini	Properties Mentioned by Kashyapa	Inference	
1	Nakini	Always delivers dead fetus.	Repeated still births	
2	Pishachi	Fetus dies immediately after birth	Early neonatal death	
3	Yakshi			
4	Aasuri			
5	Kali			
6	Varuni			
7	Shashti			
8	Bhiruka	Neonatal death from		
9	Yamya	day 2nd to 15th day	Neonatal	
10	Matangi	/ respectively	death	
11	Bhadrakali	and a second		
12	Raudri			
13	Vardhika	3441 MAPE 4218		
14	Chandika	5741		
15	Kapalaalini]]		
16	Pilipichchhika]/		

Asadhya Jataharinies: These are eight in number

No.	Name of Jataharini	Properties mentioned by Kashyapa	Inference
1	Vashya	Repeated intra-uterine death of fetuses in 5^{th} , 6^{th} or 7^{th} month.	Intra uterine death
2	Kulakshayakari	Woman whose sons die and daughters survive even without proper care	-
3	Punyajani	Children of the afflicted woman die immediately after birth.	-
4	Paurushadini	Progeny die before attaining the age of sixteen years	Some hemolytic disorders
5	Sandamshi	Immediately after conception the child born just before this conception dies.	-
6	Karkotaki	When conceives her one child(of twins) dies and another suffers from <i>Balagraha</i>	Twin pregnancy complications
7	Indrawadawa	Woman who's one or both the children of twin delivery die.	Twin pregnancy complications

Int. J. Ayur. Pharma Res	earch, 2020;8(Suppl 2):95-102	
8 <i>Badawamukhi</i> When one child of o first and subsequent		n pregnancy plications
Clinical features ^[10] after affliction of Jataharinies	2. Secondary Antiphospholipid	syndrome:
Due to affliction of Jataharini the woman get		-
withered and has these clinical features:	3. In Catastrophic APLA (rare):	
1. <i>Drishtivyakulataa</i> : Woman suffers from bewildered looks.		
2. Yathaakaalam na pushyati: She suffers from		
absence of nourishment in appropriate time.3. <i>Bhrashtasatva</i>: She suffers from unsteadiness of Psychology (<i>Satva</i>).	Rare antibodies to Phosphotidyl	
 4. Nirutsaahaa: She suffers from absence of enthusiasm. 	of Which is not an APLA antibody? A) Anti Ro	
5. <i>Kukshishoola</i> : She suffers from pain in abdomen	,	
6. Bhavatya Apriyaroopa: She suffers from	-	
disagreeable looks.	A) Lupus Anticoagulant (LAC)	
7. Roghah upadruta: She suffers from variou	B) Anticardiolipin Antibodies	
disorders. 8. <i>Vipareetasamaarambha</i> : She commences ever	C) Anti Data 2 alwaannatain a	
work in opposite way.	D) Other antibodies	
9. Vipareetanishevanee: She consumes opposite of	r [A] Lupus anticoagulant (LAC)	
non-congenial edibles.	• LAC is characterized by a	prolonged partia
10. <i>Vaidhavya</i> : She becomes widow.	Thromboplastin time and particular	
11. <i>Ayashah</i> : She faces failure at every work and los of wealth.	canca anticoaguiant is a po	werful thromboti
12. Kulakshayakari: Jataharini after seizir	agent in vivo.	
destructs her family.	• Higner thrombotic potential	than ACL when
Chikitsa ^[11] of Jataharinies	present alone.	function causing
1. Avasinchan of afflicted woman by the woma	 LAC interferes with platelet aggregation & thrombosis a 	
from whom she got Jataharini	with endothelial function, cau	
2. Prajavaran Bandha	JAPR activation & thrombosis.	
3. Putrakameshti Yajna	Prevalence of LAC in	
Brief Review of Antiphospholipid Antibod	y \succ Low risk population is < 1%	1
(APLA) Syndrome	➢ Bad obstetric history - 9.1%)
• Antiphospholipid syndrome or antiphospholipid	\checkmark Early DEPENDING = 1070.	
antibody syndrome (APS or APLS or Huges) is a autoimmune, hypercoagulable state caused b	\rightarrow //hrunfion - 330/2	
antibodies against cell-membrane phospholipic		sus - 34%.
that provokes blood clots (thrombosis) in bot	F=3 · · · · · · · · · · · · ·	ACL)
arteries and veins as well as pregnancy-relate	ACL were thought to react against Cardiolipin but	
complications such as miscarriage, stillbirt	0	
preterm delivery, or severe pre-eclampsia.	• 85% of APS patients have both	
 The syndrome occurs due to the Autoimmun production of Antibodies against Phospholipi 	1	
(APL) of the cell membranes.	bereens for the presence of	• •
 Patients have laboratory evidence for Antibodie 	dependent Anticardiolipin anti	Doules (ACA)
(IgG, IgM or IgA) against Phospholipids of		
Phospholipid- binding protein cofactors in the		1% of APS nations
blood.	and commonly with others.	1 /0 01 AI 5 Patiellu

Types of APLA Syndrome- Four types-

1. Primary Antiphospholipid Syndrome (PAPS):

When APS occurs in the absence of any other related disease (LA, ACL antibodies in patient's serum).

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and commonly with others.

• Binds to B2GP1 disrupting f(x).

B2GP1 has anticoagulant activity through the

inhibition of the conversion of Prothrombin

Thrombin, regulation of protein S, & /or activation of platelets.

Thrombophilic defects- Either Acquired or Inherited

Thrombophilia- Tendency to thrombosis.

[1] Acquired APLA

- 1. Lupus anticoagulant antibodies
- 2. Anticardiolipin antibodies
 - Myeloproliferative diseases
 - Malignancy
 - > Paroxysmal nocturnal Haemoglobinuria
 - Nephrotic syndrome

[2] Inherited APLA

- Hyperhomocysteinemia (C677T) mutation
- ✤ Factor V Leiden mutation (A506G) mutation
- Mutation in Prothrombin (G 20210 A)
- Prothrombin II (PTII) mutation
- Protein S deficiency
- Protein C deficiency

All these conditions should be investigated for APLA except

- A.) Early onset severe Pre- Eclampsia
- B.) Arterial or venous thrombosis
- C.) Unexplained fetal growth restriction
- D.) Gestational Diabetes

Diagnosis of Apla

- Due to fluctuating titers of the antibodies,
- Lack of agreement between laboratories concerning standardization of the assays,
- Debates among researchers and clinicians concerning which antibodies to measure.

Pathology

Pregnancy losses classified as:

- Occult (preclinical or chemical) pregnancy loss prior to missed menses. (40% of implantation embryos)
- Early pregnancy loss before 12 week (13%)
- Late pregnancy loss after 12 week (1%)

Causes of pregnancy loss:

- **Chromosomal-** 55% of occult & early losses 5% of recurrent losses.
- Environmental-
- 1. Immunological- It includes 5% of early losses and 95% of late losses.
- 2. Anatomical
- 3. Hormonal

What is Recurrent pregnancy loss? What actually causes it?

• A Recurrent pregnancy loss (RPL) is three or more consecutive, spontaneous pregnancy losses,

under 20 weeks of gestation from the last menstrual period by the same partner.

- "Primary recurrent pregnancy loss" refers to couples that have never had a live birth.
- "Secondary RPL" refers to those who have had repetitive losses following a successful pregnancy.

Primary Antiphospholipid Antibody Syndrome Presentation may be totally asymptomatic or in a classical manner

Various clinical presentations,

- Recurrent pregnancy loss
- Unexplained second / third trimester loss
- Early onset severe pre-eclampsia
- Arterial or venous thrombosis
- Unexplained fetal growth restriction
- Prolonged coagulation studies
- Autoimmune diseases
- Cardiac valvular diseases
- Neurological disorders
- Thrombocytopenia

Sapporo Criteria (updated)

Pregnancy Criteria

- One or more unexplained fetal deaths > 10 weeks of pregnancy.
- One or more Pre-eclampsia/Eclampsia or placental insufficiencies occurring before 34 weeks.
- Three or more unexplained consecutive spontaneous abortions < 10 weeks.</p>

Laboratory criteria

- ✓ LAC defined by a functional, clot-based assay (ISTH guidelines)
- ✓ ACL (IgG or IgM) antibody
- ✓ Anti-Beta-2 Glycoprotein 1, IgG or IgM antibody (Miyakis, et al., J. Thromb. Haemost., 2006; 4: 295-306).

Management

Controversies surrounding treatment for pregnancy loss

Evidence-based medicine (EBM) has not succeeded in giving patients and physicians, the data they need to choose (or not choose) a therapy in the field of pregnancy loss.

How to proceed?

- Interview the couple together
- History of the case is very important
- Clinical examination
- Investigations as per the history
- Reassurance and Counseling

- Treatment plan: Drugs, maternal and fetal surveillance, dealing with complications.
- Timely referral to a tertiary centre.

So how does one manage the drug treatment in pregnancy?

General guidelines for anticoagulation in Pregnancy with APS leading to recurrent pregnancy loss is very controversial issue.

Commonly used Drugs

• Steroids: Reduces ACA, normalizes prolongation of invitro coagulation.

Complications?

Perinatal outcome, preterm labour, pre-eclampsia.

- Low dose Aspirin (LDA): Selective inhibition of Thromboxane A2 and no effect on PGI2.
- Azathioprine
- Warfarin

Which is the commonly used drug for APLA?

- A) Progesterone
- B) Folic acid
- C) Low dose Aspirin
- D) RU- 486

Unfractionated Heparin (UFH)

- Potentiates complex formation with AT III + factor VII A → XII A & Thrombin
- **Complications**: Reduces platelet bleeding and B.M.D.

Low molecular weight Heparin (LMWH)

- Once daily dose, less monitoring
- Lesser Osteopenia, does not cross placenta
- Cost factor.

Trials

• Heparin vs Aspirin + prednisolone

Live birth 75%

Pre-eclampsia, preterm delivery more in latter group.

- L.S. + LDA Vs Heparin + LDA (n=20)
- No placebo
- Large multicentric trials needed (Cowchock et al .1994)

DISCUSSION

Pregnancy loss in the APLA syndrome

Both *Jaataharini* and APLA syndrome are silent killers of fetus inutero. The presence of APL antibodies will be detected usually when recurrent pregnancy loss occurs, which indicate that this is not a routine investigation in ANC. This will be the drawback for good fetal outcome. It is not precisely known how these antibodies cause damage, but it is likely that their actions are multifactorial. Ayurveda explains that for formation of *Garbha*, *Panchamahabhuta* and *Beeja* plays an important role. Both will be strongly influenced by *Beeja dosha* and *Daiva*. APLA starts with the pathology at the level of cell immunology and mainly genetic mutations, so Ayurveda explained some references related with fundamental factors.

Role of *Panchamahabhuta* in Formation of APLA^[12,13,14]

There is no direct reference related to the Pathophysiology of *Jataharinies*, so by considering the basic fundamentals we can postulate *Samprapti* like this

- *Panchamahabhutas,* the basic entities in our body are responsible for establishment of structural and functional aspects.
- *Sushruta* says "*Apratihanana*" i.e., continuation of normal functions is the property of *Panchamahabhutas* like *Kayakriya, Vakkriya*, also *Garbhakriya*.
- *Dhamanies* carry these *Mahabhutas* in whole body and Dalhana clarifies that when the time of destruction comes first these *Dhamanies* will play a key role.

Role of *Rakta Dushti* in formation of APLA^[15,16,17]

According to Sushruta Samhita we can observe that Rakta and Artava are having similar properties. Sushruta states that "Rakta Lakshanamartavam Garbhakrichcha". Dalhana commenting on this says that Cha means all the functions of Rakta are also carried by Shuddha artava.

- The effects of large amounts of estrogen, progesterone, and prolactin must be considered. For example, Estrogens up-regulate and Androgens down-regulate T-cell response, and a number of cytokines are regulated by sex hormones. (Lockshin and Druzin, 1995; Refojo and colleagues, 2003)
- Lockshin (2002) postulates a modulating effect of hormones rather than a causative role.

Role of Kapha Dosha^[18] in Formation of APLA

(According to Su.S. Shareera)

In the pathology of APLA we have seen the role of Thrombogenesis which we can observe in *Sushruta's* opinion. *Bahala* i.e., clotting and *Gairikodaka Prateekansham* which is nothing but normal consistency of *Rakta* are brought by normal *Kapha*. In pregnancy normal physiological hematological changes like increased plasma volume may lead to production of thrombotic agents and antibodies.

Kapha Bahala (clotting) and *Gairikodaka prateekansham* (the more plasma, which leads to the

production of Annexin V and antibodies). *Mamsa, Peshee, Prabham* means clotting. (Su.S. Sutra.14/21)

B-2 Glycoprotein 1 and Kapha dosha

 B-2 Glycoprotein1 (Apolipoprotein H) Kapha being same property.

Proteins are anabolic agents.

- B-2 Glycoprotein 1 more on the surface of the syncytiotrophoblast.
- B-2 Glycoprotein 1 inhibits clotting factors (Factor XII) and prothrombinase complex.
 - B-2 Glycoprotein may be involved in implantation because it is known that, this protein binds Heparin. Moreover, trophoblastic cells have Heparin like binding sites.
 - So, *Kapha dushti* cause accumulation of clotting factors in *Rakta dhatu* by allowing the Factor XII, Prothrombinase and preventing from binding with Heparin.
 - So fall in B-2 glycoprotein might prevent implantation or result in intervilleous space thrombosis or both.

Role of *Ojas*^[19,20] (Immunity) in Formation of APLA

- Immunity in the aspect of Ayurveda is considered under *Ojas*. Sushruta states that if *Ojas* is absent, body tissues start to degenerate. Charaka clearly says that in *Garbhavastha* the *Ojas* is present in three forms
- 1. Before the formation of *Garbha* ie, *Saara* of *Shukra* and *Shonita* act as *Ojas*.
- 2. After formation of *Kalala* i.e., embryo in the form of *Rasa Saara*.
- 3. During the organogenesis in the form of preventive cell layer or tissue layer.
- The immune system is designed to protect cells, tissues, and organs perceived as self and to attack and destroy foreign or none self antigenic material by the production of antibodies. This protection has two phases:
- Innate phase, which is broad and rapid and is mediated through Neutrophils, Macrophages, and complement.
- Adaptive phase, which is precise and is caused by antigen-specific reactions through T and B lymphocytes that result in memory for future exposures (Parkin and Cohen, 2001).
- The immune system may be stimulated to begin producing antibodies directed against self or normal tissues. These misdirected antibodies are called Auto-antibodies. The stimulus responsible for their production is unknown, but a variety of inciting reasons are suspected that include bacterial or viral injury to genetically susceptible

tissues. Aggravated *Vata dosha* guides this phenomena with its property. As explained by *Charaka acharya* in (Cha. Su. 12/8) like,

Vaay ust antray antra dharah.....Karta agarbhak riteena ||

- Auto-antibodies induce destruction in susceptible tissues by at least two mechanisms:
- ✓ The cytotoxic mechanism involves direct antibody attachment to a specific surface antigen, which results in cell injury or destruction.
- ✓ The immune-complex mechanism results in tissue damage when the antigen–antibody complex attaches to a susceptible tissue.

Samanya Chikitsa Sutra

- 1) Garbhini Paricharya
- 2) Hygiene
- 3) Timely treatment for minor ailments.
- 4) Psychological support
- 5) Pumsavana
- 6) *Kledahara oushadhi prayoga* especially in 2nd trimester
- 7) Daiva vyapashraya chikitsa

CONCLUSION

Both Jaataharini and APLA syndrome are silent killers of fetus in utero. The presence of APL Antibodies will be detected usually when recurrent pregnancy loss occurs, which indicate that this is not a routine investigation in ANC. This will be the drawback for good fetal outcome. It is too difficult to draw accurate correlations and aetio-pathogenesis of *laathaharini* because of unavailability of full version of Kashyapa Samhita and no references in Brihatrayees. Only on the basis of unexplainable mode of onset of syndrome and fetal recurrent losses explained under this context, I tried to correlate these explanations under APLA syndrome. In cases of adverse pregnancy outcomes APLA should be kept in mind. The only intervention to have demonstrated benefit is serial ultrasound scans in early months of pregnancy. For patients with APLA/ Thrombophilia, referral to a tertiary unit as multidisciplinary management is required. Psychological support is required. Couple should be counselled together. Education and reassurance has an important role to play.

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Cite this article as:

Sushma. Critical Analysis of Jataharinies Wsr To Antiphospholipid Antibody Syndrome. International Journal of Ayurveda and Pharma Research. 2020;8(Suppl 2):95-102.

Source of support: Nil, Conflict of interest: None Declared

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