The Mumbai Obstetric & Gynecological Society

MOGS NEWS & VIEWS

THEME : RECURRENT PREGNANCY LOSS

Volume III - Dec. 2021

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Presidents Message

Dr. Sarita Bhalerao
President MOGS

Dear MOGS Members,

It gives me great pleasure to bring you this News & Views on Recurrent Pregnancy Loss. RPL is an important reproductive health issue. It is a challenging area with many uncertainties. Common established causes include uterine abnormalities, antiphospholid antibodies, cytogenetic causes, endocrine abnormalities. Other etiologies have been proposed but remain controversial like chronic endometritis and male factor abnormalities. Over the years many evidence based treatments have improved outcomes but still many treatments remain empirical. RPL is a cause of much distress to the affected couple and we gynecologists have to counsel them carefully. Most couples do however achieve a healthy live birth.

I would like to congratulate the editors Dr. Kedar Ganla, Dr. Sanket Pisat, Dr. Madhuri Mehendale , Dr. Mansi Medhekar and the entire editorial team for bringing out this excellent issue with all the recent updates.

MOGS is honoured to have 2 new patrons, Dr. Aspi Raimalwala and Dr. Priti Vyas. I thank them for their generous contribution.

Our MOGS website has been refurbished and made dynamic and user friendly. Dr. Suvarna Khadilkar and her team have worked very hard to make the new website live in a short time. Do log onto www.mogsonline .org and send us your feedback.

Our monthly quiz program on the MOGS app is now very popular. Dr Punit Bhojani has put a lot of effort into this.

MOGS prizes and awards for 2021-2022 have been announced and all the details are on our website. This year we have introduced one new prize for the best thesis on fetal medicine. This has been done through a generous donation by Dr. Ajay Mehta in the name of his father, the late Dr. Ajit Mehta.

I am delighted to announce the **MOGS – Dr. Duru Shah Outstanding Youth Award.** This will be awarded to a young MOGS member for their outstanding performance in the areas of academics, extracurricular activities and social work. In addition , they will be judged based on an essay on the topic of `Climate change its effect on health and what India can do`.

On the social front, MOGS pledged to make India anaemia free. This program was coordinated by Dr. Komal Chavan. Video messages were uploaded to create awareness about Violence against women through the efforts of Dr. Reena Wani.

Our next program is **`New vistas in Gynaecological Oncology`**. Dr. Neerja Bhatla , renowned gynaec oncologist and Professor and HOD at AIIMS, New Delhi will deliver the prestigious ` MOGS- Dr Subhash Penkar Dr Marie Perreira Oration`. Dr. Shailesh Puntambekar world famous Laparoscopic surgeon will deliver a keynote address on `Laparoscopy in Gynaec Oncology`.

Please do join us for the **Youngistan Conference** on Saturday, 05th February, 2022. Youngistan was started by Dr. Rishma Dhillon Pai in 2021. The Faculty will be young MOGS members below age of 40 years. We will also be conducting the MOGS Dr. Hrishikesh Pai& Dr. Rishma Pai quiz for 2021 - 2022.

This year the **MOGS –Dr. Shirish Sheth preconference workshop** will be held on 20th February 2021 in Ghatkopar. The theme of the workshop is ` Pelvic Floor`. In addition we will have 2 more workshops , one on Hypertensive disorders in pregnancy and another on fetal medicine.

Our **Golden Jubilee Annual Conference** will be held on February 26th – 27th, 2022 at Hotel Trident, Nariman Point, Mumbai. Please do block your dates and participate. A galaxy of stalwarts will participate as faculty . We are delighted that Dr. S.Shanthakumari , FOGSI President will be our Chief Guest.

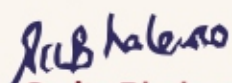
Our **MOGS Dr. Nandita Palshetkar Post Graduate intensive training program** will be held on March 23rd to 27th, 2022 at Sion Hospital.

We also have outreach programs planned in different locations.

In March 2022 MOGS plans to celebrate International Womens Day with week long programs on womens health in the form of camps and public awareness sessions.

No matter how hard the past, you can always begin again- *Buddha*

As 2021 draws to a close I would like to wish everyone best wishes for the new year. 2021 was a testing year . We as a community came together to fight the COVID virus. We have emerged stronger. Let`s welcome 2022 with positive thoughts and hope.



Dr. Sarita Bhalerao.
President, MOGS

Secretaries Message

Dr. Suvarna Khadilkar
Secretary MOGS

Dear friends,

Greetings from MOGS HQ!!! we are extremely glad to present to you this third issue of news views 2021-22, focussed on Recurrent Pregnancy Loss (RPL)

Spontaneous pregnancy loss is a surprisingly common occurrence. Approximately 15% of all clinically recognized pregnancies result in spontaneous loss, there are many more pregnancies that fail prior to being clinically recognized. Only 30% of all conceptions result in a live birth. Rest of the pregnancies are lost; this can be physically and emotionally taxing for couples. The experience of pregnancy loss can be so heart-breaking, and the grief is hard to navigate because it's so imperceptible.

"You never arrived in my arms, but you will never leave my heart." — Zoe Clark-Coates

These words depict the exact emotion that couple goes through after a pregnancy loss. Hence, we must understand that the tender loving care and counselling become vital in management.

I applaud the efforts of Dr. Kedar Ganla, Dr. Sanket Pisat, Dr. Madhuri Mehendale , Dr. Mansi Medhekar, and the whole editorial team. The topics chosen for the articles are all very important. They include unexplained RPL, autoimmune causes, alloimmune factors, genetic factors and anatomic factors implicated in RPL.

This issue gives outline of the upcoming programs and detailed report of our very successful MOGS AMOGS hybrid conference held on 16th 17th October. Apart from this major event we organised five physical outreach activities, and many more online webinars on different important topics. Please note that the last date for applications for MOGS awards is 31st December, do apply and get recognition for the amazing work that you all are doing.

We are glad to announce that we launched our new website on 20th November at our program on current guidelines at hotel Courtyard Marriot!! It now has a new avatar and is totally revamped. We have changed its format from static to dynamic type. Navigating the website is now more user friendly. We have included separate tabs for our MOGS activities, membership, post graduate teaching, and also for our community activities on home page.

I sincerely hope that you enjoy the experience of browsing our new website. we are also pleased to inform you all that keeping abreast with new trends and needs of the modern days and age, we are now on twitter, Instagram and Facebook. We have our own you tube channel and google photos accounts as well. Events in Mumbai and the whole MOGS team worked tirelessly for streamlining the website and other social accounts. Also use following links to access our newly started social media accounts. Please like, follow, and share to your friends to disseminate MOGS activities.

Website	www.mogsonline.org.
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Facebook	https://m.facebook.com/Mogs_HQ
Instagram	https://www.instagram.com/mogshq
You Tube	https://www.youtube.com/channel/UCMneZsGY3fgr0wawvfZcXXA

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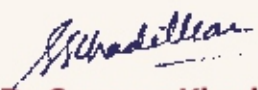
Last few months we did have some relief from the covid restrictions and we could meet our friends at physical meetings. I wish that we continue to meet like this in future and I wish you a very happy and healthy new year 2022!

LONG LIVE MOGS!!!

With warm regards,



Dr. Suvarna Khadilkar
Secretary, MOGS

Editorial

Dr. Kedar Ganla
Editor

Dr. Sanket Pisat
Editor

Dr. Madhuri Mehendale
Editor

Dr. Mansi Medhekar
Editor

Dear MOGS Members,

The MOGS newsletter has been our most important academic activity.We aim for practical topics that our members can keep at hand for reference .

We have tried to keep it as algorithmic and practical as we can .It with great pride that we bring to you our newsletter on Recurrent Pregnancy Loss. We have tried to compile the most commonly seen scenarios to practical counselling tips ,clinical evidences ,recent guidelines and publications related to the topic.

We thank our MOGS President Dr Sarita Bhalerao and the officebearers for entrusting us with this responsibility.We have tried our best to be innovative and as practical as possible.We hope our members enjoy reading this as much as we did while compiling these aspects of Recurrent Pregnancy Loss.We would like to hear from our members any suggestions that can help us further improve our newsletter in future.

Wishing you all a safe and healthy time ahead !

Dr Kedar Ganla

Dr Sanket Pisat

Dr Mansi Medhekar

Dr Madhuri Mehendale

Unexplained Recurrent Pregnancy Loss

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Dr Priyanka Vora
(DGO, DFP, MRM)

Introduction -

Unexplained recurrent miscarriage (RM) is an extremely challenging and frustrating condition for both clinician and the patient affecting approximately 40% to 50% of all miscarriages. Further, there is no diagnostic test or concrete evidence-based management currently available.

Fig 1 : Causes of recurrent pregnancy loss

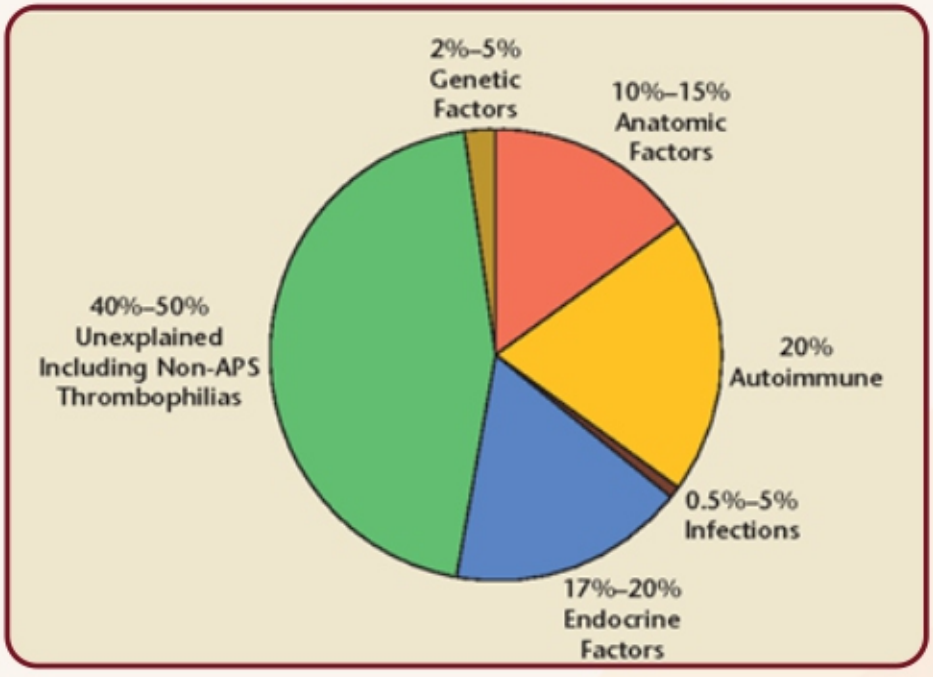

Table 1: Salient feature about unexplained recurrent pregnancy losses (URPL)

- URPL is considered the diagnosis if a complete genetic, anatomic, endocrine, and immune evaluation was performed and returned as normal.
- Couples with URPL should be informed that the chances for a future successful pregnancy could be as high as 50%–70% and depend mostly on maternal age and number of previous losses.
- Women aged 30 years are estimated to have a 75% chance of live birth within 2 years, compared to 40% for women aged 40 years.
- In women with 3 miscarriages, the chance of a future live birth within 2 years is 70%, compared to 45% following 6 miscarriages.
- Several studies have reported a genetic predisposition to URPL, with an increased risk in siblings of patients with URPL.
- A successful pregnancy depends on immune balance, and interleukins secreted by immune cells play important roles in that balance at different stages of implantation.
- Interleukin genes IL-1, IL-6, IL-10, and IL-18 are the most commonly associated with RPL.
- There is insufficient evidence to recommend management based on HLA phenotypes.

Could all unexplained RMs be chance occurrences?

Around 1:3, may have significant environmental risk factors or endogenous pathologies, not detected by current routine investigations due to:

- Obesity, smoking, alcohol, caffeine and exposure to certain occupational hazards,
- Immunological pathology,
- Endocrinological and endometrial abnormalities,
- Impaired decidualization of the endometrium.

OOCYTE FACTOR

- Ageing
- Poor ovarian reserve
- PCOS
- Aneuploidy is the main cause in women with ↑ age
- Premature ovarian aging –↓ oocyte quality & quantity
- Anti-Mullerian hormone & Estradiol were significantly ↓ in women with idiopathic recurrent miscarriage

Management options –

1. Dehydroepiandrosterone (DHEA) – Studies have shown that women undergoing IVF who received 75 mg of DHEA daily (25 mg TDS) for 17.6 +/- 2.13 weeks had a significant high rate of fertilized oocytes (P < 0.001), day 3 embryos (P = 0.001), embryos transferred (P = 0.005) and average embryo scores per oocyte (P < 0.001).9

2. Antioxidants- Cochrane Database Syst Rev. 2017 states that there is very low-quality evidence to show that taking an antioxidant may provide benefit.

SPERM FACTOR:

The Sperm
- Y chromosome Microdeletion
- Sperm oxidative stress
- Sperm DNA fragmentation
- Sperm concentration/ motility
- Sperm Morphology

Investigations
- Semen analysis
- Sperm function test
- Sperm DNA fragmentation
- Sperm FISH – Sperm aneuploidy
- Blood sugars

high Sperm DNA fragmentation is a major contributor to URPL.

Management options-

- Antioxidants – Oxidants damages plasma membrane of sperm leading to lipid peroxidation and DNA Fragmentation. These lead to decrease fertilization rate and early abortions. The Cochrane Database Syst Rev. of 2017 says that there is low quality evidence suggesting that antioxidant supplementation in subfertile males may improve live birth rates.

EMBRYO FACTOR:

The Embryo
- PGS of embryo for aneuploidy in women with RPL ?
- Lack of RCTs
- IVF & PGS needed ? Cost?

IVF-PGD should not be offered first-line, given the unproven benefits, additional cost & potential complications associated with ART.

ENDOMETRIAL FACTOR:

The Endometrium

- Endometrial thickness, Vascularity
- Receptivity ?
- Women with RPL have increased levels of proimplantation cytokines

Studies on the endometrial vascularity and receptivity in URPL patients in the midluteal and early pregnancy phases showed that endometrial thickness, endometrial volume, endometrial vascular data, VI, FI, and VFI of the midluteal phase were lower in the URPL group.

Management options -

1. Angiogenesis plays critical role in various female reproductive processes. Some drugs like aspirin, glyceryl trinitrate, angiogenic growth factors & sildenafil citrate have shown good effect on endometrial perfusion. There seems to be decreased endometrial vascularity in patients with antiphospholipid antibodies-associated presenting with URPL.
2. There seems to be an association between chronic endometritis and URPL. The per-pregnancy LBR for the treated chronic endometritis group was 7% (7/98) before treatment versus 56% (28/50) after treatment in a study.

Role of surgical correction -

In a study on 56 patients with low uterine cavity and T shaped uterus, metroplasty by office hysteroscopy was done. Hysteroscopic treatment significantly increased volume of uterus and 80% conceived.

Management options -

1. Heparin - A study on resistance of uterine radial artery blood flow and its correlation with peripheral blood NK cell fraction (2015) showed improved pregnancy outcome with LMWH.
2. Aspirin – Low-dose aspirin showed a highly significant reduction in PI & S/D of uterine arteries.
3. Immunoglobulins - Current evidence is insufficient to support the beneficial effects of IVIG on an URPL.

Other factors Unexplained RPL

- Environmental
- Obesity
- Role of Vit D?
- Role of folic acid?
- Stress?
- Micronutrients?

Obesity

A meta-analysis (2018) found that obese women with a history of RPL have a high risk of future pregnancy losses and euploid miscarriages.

Progesterone supplementation

- A meta-analysis of 10 RCTs (1,586 women with URPL) found a significantly lower risk of recurrent miscarriage and a higher chance of live birth with progesterone.
- Synthetic progestins were found to be beneficial, whereas natural and micronized progesterone had no impact.

Other management options

- Intralipids have immunomodulatory properties and act by inhibiting NK cell activity.
- One RCT found that G-CSF administration significantly increased LBR in women with URPL.
- Larger multicenter trials are needed before recommending G-CSF or intralipids use in clinical practice.

Conclusion

Various etiologies have been identified for URPL and successful therapeutic strategies implemented. Lifestyle modifications should be advocated as almost 50% of cases remain unexplained. A thorough follow-up with an important psychological support can help most couples achieve a successful live birth.

Autoimmune causes of RPL

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Treasurer-MOGS

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Managing Council Member MOGS

Dr. Garima Sharma
Senior ART Consultant
at Apollo Fertility, Mumbai
Youth Council Member MOGS

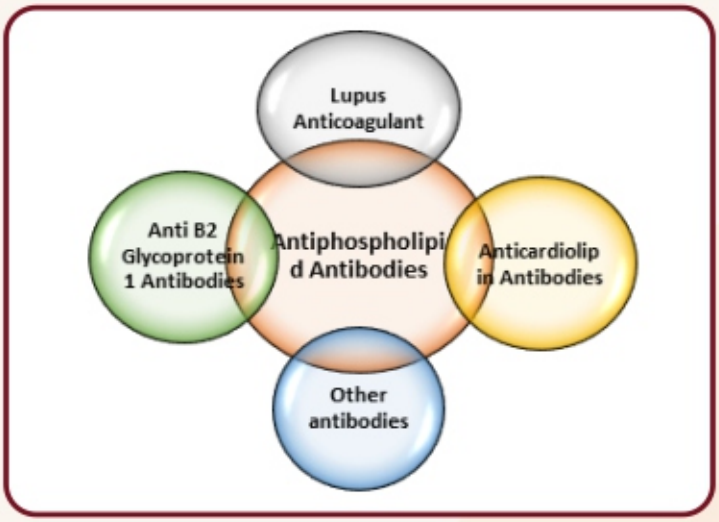
Autoimmune Causes of RPL

It accounts for about 15 – 20% of RPL causes. The most common autoimmune causes of RPL are:

1. Antiphospholipid antibodies syndrome (APLA)
2. Antinuclear antibodies
3. Antithyroid antibodies

Antiphospholipid antibodies syndrome (APLA)

APS is an autoimmune condition characterized by the production of moderate to high levels of antiphospholipid antibodies and certain clinical features. The presence of these antibodies during pregnancy is a major risk factor for adverse pregnancy outcome.



Classification

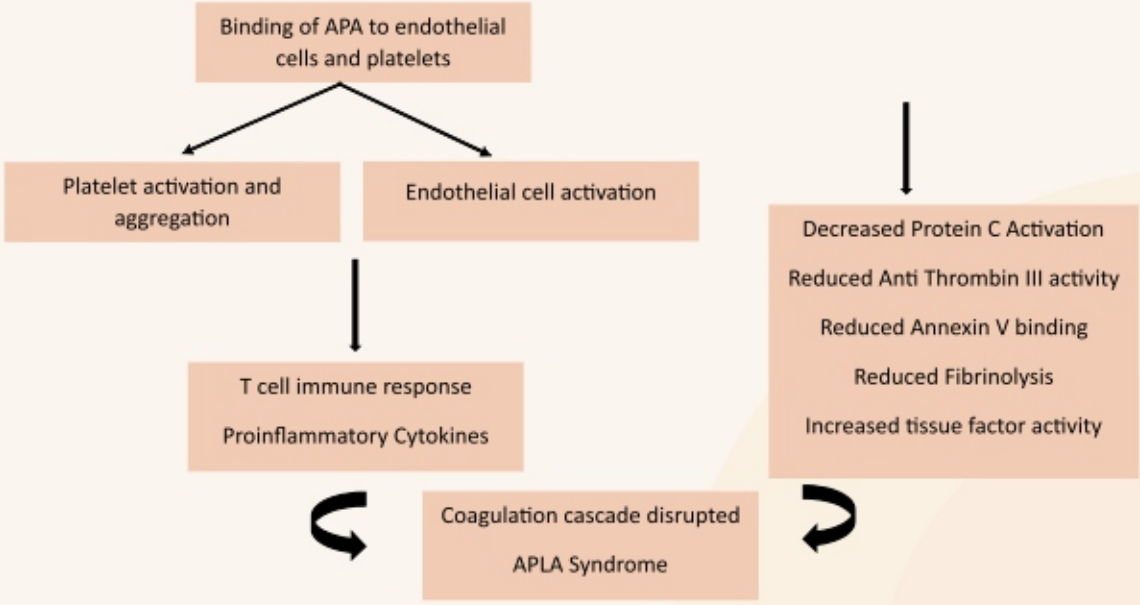
APLA

- Primary: APS occurs in the absence of any other related disease. (ACL, LA antibodies in patient serum)
- Secondary: APS coexists with other disease like SLE
- Catastrophic: Rare event. Generalized thrombosis leads multiorgan failure and high mortality

Mechanism of action

1. Interferes with the coagulation cascade
2. Abnormal decidualisation by inhibiting PRL and IGFBP-1 production by Endometrial stromal cells
3. Abnormal trophoblast function – poor invasion & hormone production. APLA inhibits the expression of trophoblast cell adhesion molecules (alpha 1 and alpha 5 integrins, E and VE cadherins).

These events may be responsible for pregnancy losses.

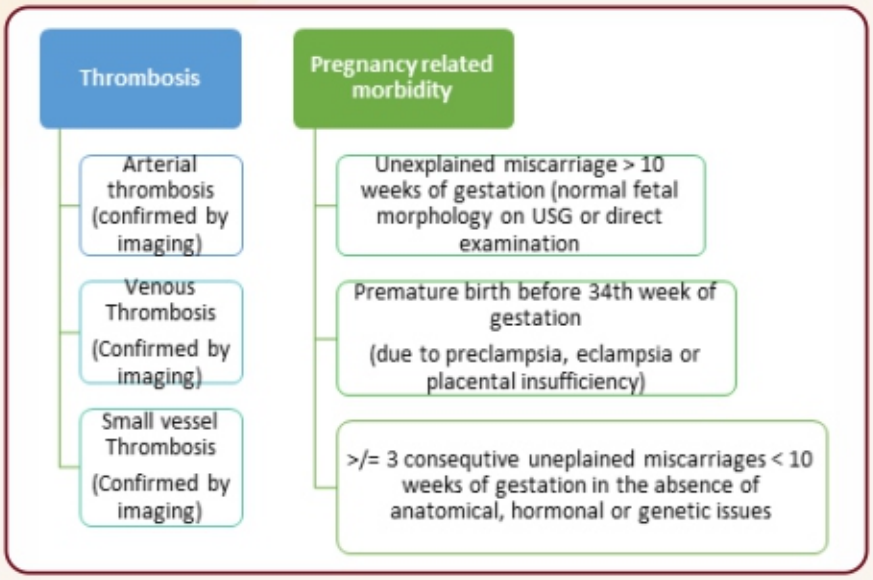


DIAGNOSIS:

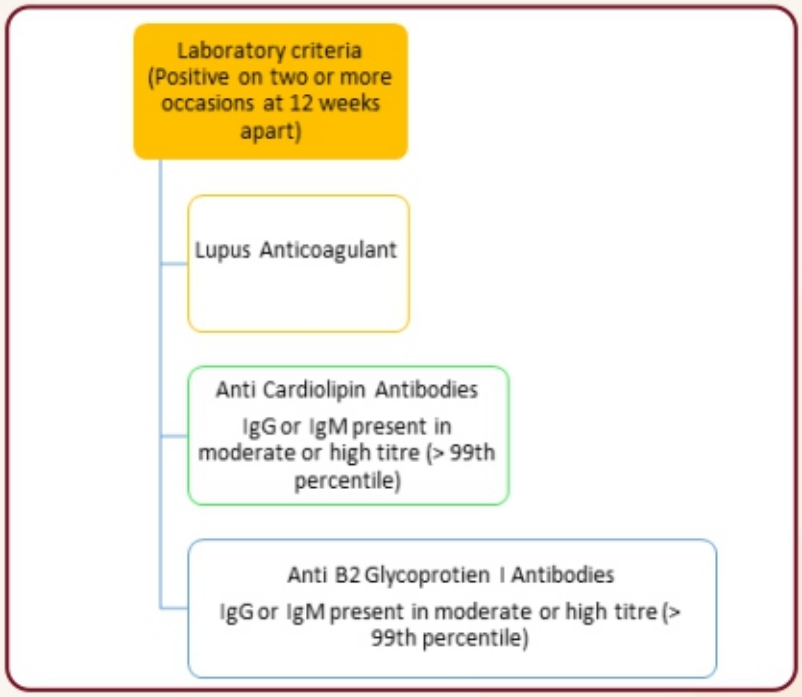
Modified Sapporo Criteria (2006)

Presence of one clinical and one laboratory criteria is required to make diagnosis

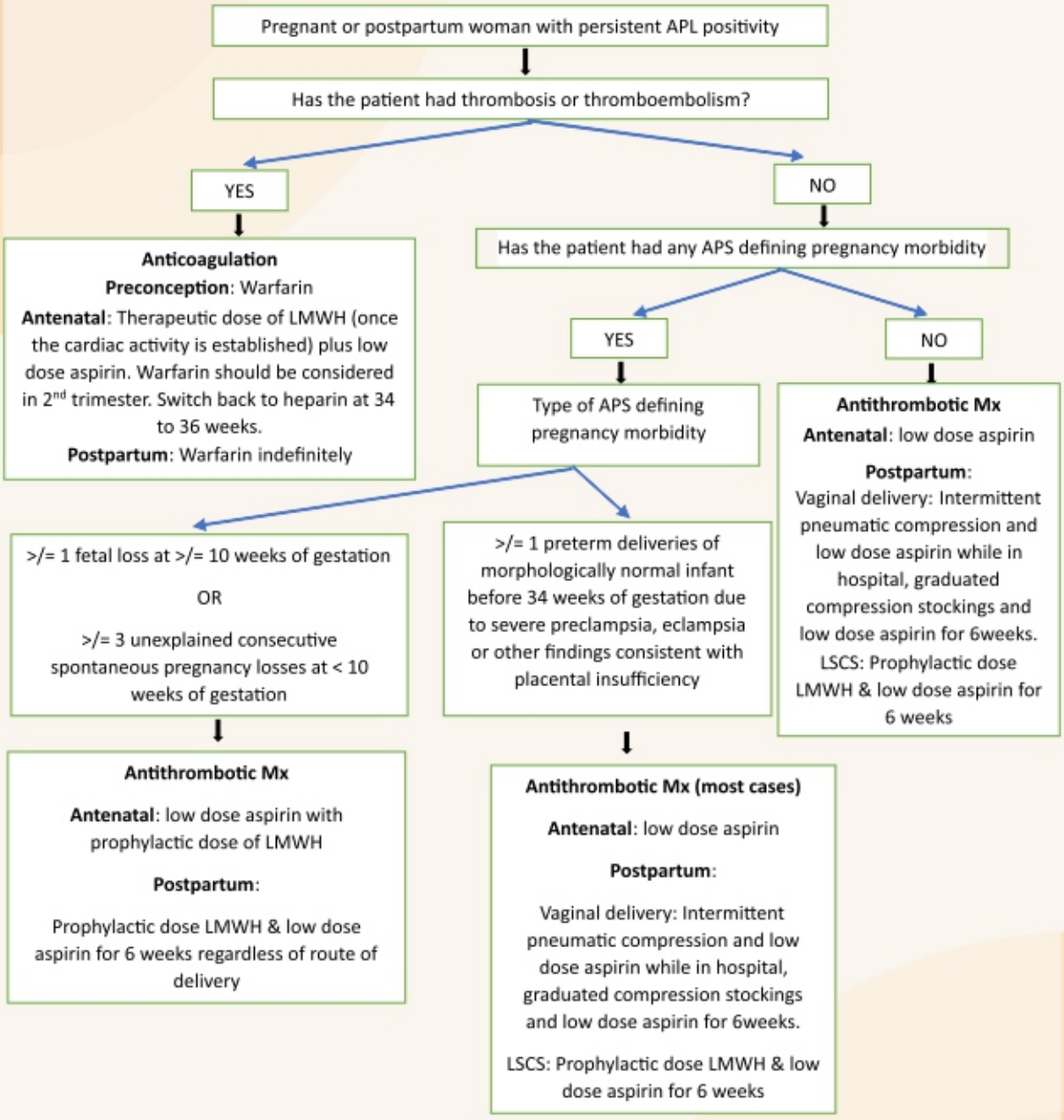
1. Clinical Criteria



2. Laboratory Criteria



Treatment Algorithm



Other Treatment Modalities

- IVIG
- Intralipid

Peripartum Management

- ACOG recommends that adjusted dose of LMWH/UFH can be discontinued 24 to 36 hrs before induction of labour or LSCS.
- Withhold neuraxial block for 12 hours for prophylactic dose and 24 hrs for therapeutic dose
- Interval to restart LMWH/UFH- 4-6 hrs hours after Normal delivery and 6-12 hours after LSCS
- Patients with history of thrombosis should not be without anticoagulants for more than 48 hrs.
- Delivery via induction of labour or LSCS at 39 weeks of gestation.

Dosing of LMWH

PROPHYLACTIC DOSE		THERAPEUTIC DOSE	
No need of monitoring		**Monitored by anti Xa levels**	
DRUG	**Dose SC once daily**	**DRUG**	**Dose SC every 12 hr**
Enoxaparin	40 mg	Enoxaparin	1 mg/kg
Dalteparin	5000 IU	Dalteparin	100 IU/kg
Tinzaparin	4500 IU	Tinzaparin	100 IU/kg

Target anti Xa levels 0.6 – 1 U/ml
Switch to UFH – 36weeks
Can start LMWH with warfarin from postpartum day 1

Actions Of Heparin:

- Anticoagulant -- Potentiates action of Antithrombin
- Non-anticoagulant actions
- Restores trophoblast invasive properties
- Restores placental HCG production
- Immunomodulation of cellular immunity, antagonizes IFN gamma production
- Heparins prevent pregnancy loss and inhibit complement activation

Mechanism Of Action of Unfractionated Heparin

Heparin binds with antithrombin (AT : natural anticoagulant protein) and changes conformation of AT

↓

Increased anticoagulant activity of AT & this speedsup the inactivation of thrombin

↓

AT slows coagulation activity by inactivating thrombin (IIa) and Xa

↓

Heparin approximately equally binds II a and X a

IVIG VERSUS HEPARIN/ASPIRIN

In a multicentric study conducted by Yamada et.al. and published in 2012; IVIG was compared with LMWH. Live Birth rate was 72.5% in aspirin + LMWH and 39.5% in IVIG group

- Used in patients with very high levels of APLA antibodies
- Intravenous immunoglobulins given every 3 weeks
- 20 G daily for 5 days. Total 100gms
- In conjunction with LMWH and aspirin

ANTINUCLEAR ANTIBODIES

Detectable antinuclear antibodies are found in approximately 10-15% of all women regardless of their history of pregnancy loss. At present, there is no conclusive opinion on the clinical impact of antinuclear antibodies (ANA) in RPL. Also, currently, routine testing for ANA is not recommended by international guidelines, except, ESHRE guideline considers testing for explanatory purpose.

A recent meta-analysis published in 2020 by Chen Shiju including 21 studies on ANA in RPL, reported a significantly higher rate of elevated ANA titres in RPL patients (22%) compared to controls (8.3%) as well as a significant association between positive ANA and a risk for RPL

The association was more evident especially with high titres (≥1:80; ≥1:160) or a homogenous ANA pattern. Therefore, the best predictive cut-off level for ANAs in RPL patients remains to be defined.

If elevated ANA titres (referred to as “above lab reference range”) are diagnosed in RPL patients, the antibodies should be further differentiated (SS-A/RO and SS-B/lupus anticoagulant (LAC)antibodies) to rule out a Sjögren's syndrome or lupus erythematosus (as a neonatal lupus syndrome could lead to a foetal AV block).

Maternal and Fetal Outcomes :

Preconception	Mother during pregnancy	Fetus
Unexplained Infertility	Increased risk of DVT or PE	Early miscarriage
Recurrent Implantation failure	Preclampsia or Eclampsia	Prematurity
Risk of DVT or PE due to hormonal stimulation	Abruptio Placentae	IUGR
	Increased Risk of thrombocytopenia	Still birth

Summary

Suggested immunological standard diagnostics.

		Suggested Procedure
Autoimmune Risk Factors	**APLS**	ACA, LAC, Anti-β2-glykoprotein I antibodies Analysis should be performed at two separate occasions at an interval of 12 weeks Consider a non-criteria APLS, if clinical manifestations are present (renal microangiopathy, neurological disorders, cardiac manifestations, or ulcerations of the skin)
	IgA Antibodies Transglutaminase	IgA antibodies against Transglutaminase should only be analyzed in women with a history of food sensitivity followed by colon biopsy if antibodies positive
	ANA	Only ANA titres >1:160 are considered as positive If the ANA titres are elevated, antibodies should be further differentiated (SS-A/RO and SS-B/ lupus anticoagulant (LAC)antibodies) to rule out Sjögren's syndrome or lupus erythematosus
	Thyroid Antibodies	TSH level should be analysed. If TSH levels are >2.5 mU/L, T3, T4 and thyroid autoantibody concentrations should be determined

Therapeutic options mentioned in different guidelines concerning immunological alterations.

	DGGG/OEGGG/SGGG (2018)	ESHRE (2017)	ASRM (2012)	RCOG (2011)
APLS Therapy	Low dose aspirin plus unfractionated heparin or low molecular heparin starting with day of positive pregnancy test. Aspirin until GW 34+0, heparin 6 weeks post-partum (APLS and non-criteria APLS)	Low dose aspirin starting before conception plus prophylactic dose unfractionated heparin or low molecular heparin starting with a positive pregnancy test	Low dose aspirin and unfractionated heparin	Low dose aspirin plus heparin

MOGS Prizes - Thesis (Deadline 31st December, 2021)

Sr. No.	Name of the Prize	Criteria	
		Subject	Eligibility
1.	**MOGS Dr H Desa Silver Jubilee Prize**	Candidate's choice	Less than five years from MMC Registration
2.	**MOGS Dr Kamal S Jain Prize**	High risk pregnancy	Less than ten years from MMC registration, Postgraduate qualification in OBGYN
3.	**MOGS Dr N K Allahabadia Research Award**	Imaging modalities in OBGYN	Age less than 35 years
4.	**MOGS Dr Pramila Bhatia Young Scientist Award**	Original work of candidate's choice / recent scientific work	Age less than 40 years
5.	**MOGS- Dr. H. S. Palep Prize**	Recurrent Pregnancy Loss	Life member of MOGS or ordinary member for 3 yrs Age less than 50 yrs Postgraduate degree or diploma in ObGy
6.	**MOGS- Dr. G. B. Belvi Prize**	Operative & emergency obstetrics	Life member of MOGS or ordinary member for 2 yrs Age less than 40 years
7.	**MOGS - Dr. Ajit Mehta Prize**	Fetal Medicine	Age less than 50 years

Alloimmunity and RPL : Immunomodulation With Progesterone

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Dr Kirti Bendre
MD, DGO

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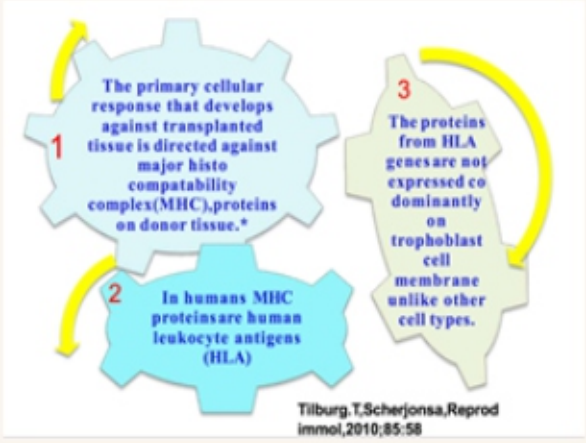
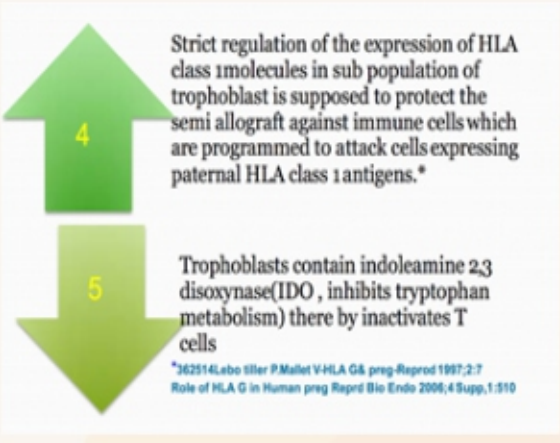
MD,MRM(UK),DRM(Germany)

Alloimmunity in Recurrent Pregnancy Loss

The immunologic nature of unexplained recurrent pregnancy loss (RPL) has generated considerable interest and controversy. Both antibody-mediated and cell-mediated mechanisms have been proposed. To date, the only scientifically validated humoral cause for RPL remains antiphospholipid antibodies (lupus anticoagulant and anticardiolipin antibodies). Most controversial in the arena of immune-related RPL is the idea that many cases are due to a maternal alloimmune response to the fetus, semiallogenic because of maternally and paternally inherited gene products and tissue-specific antigens.

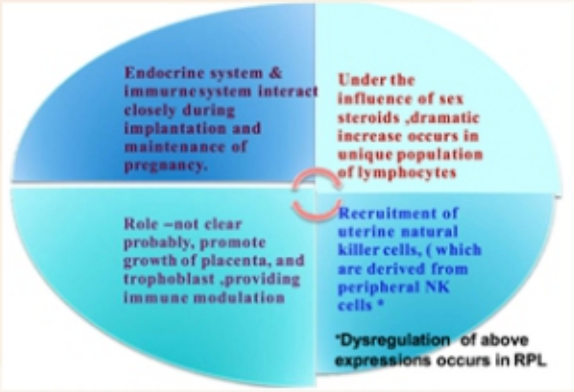
Reproductive Immunology :
Protective mechanisms in pregnancy:

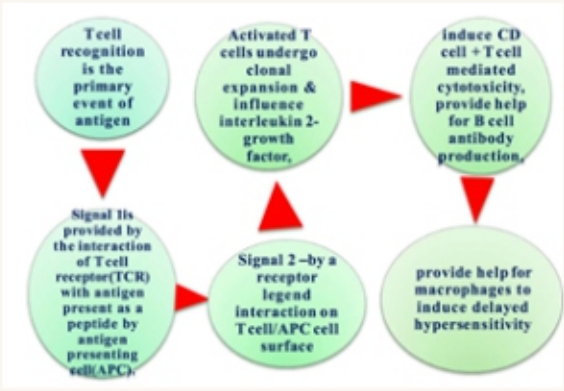




Expressions and Reactions At Fetomaternal interphase by placenta & fetal membranes

Immune Response





Alloimmunity :

- Immune response to foreign antigens (alloantigens) from members of the same species.
- The body attacks especially transplanted tissue and even the fetus in some cases.

Alloimmunity in RPL :

- In some pregnancies, the mother recognises these foreign paternal antigens and sets up an immune rejection reaction to them, which causes abortion.
- In habitual abortion, this reaction is repeated in every subsequent pregnancy.

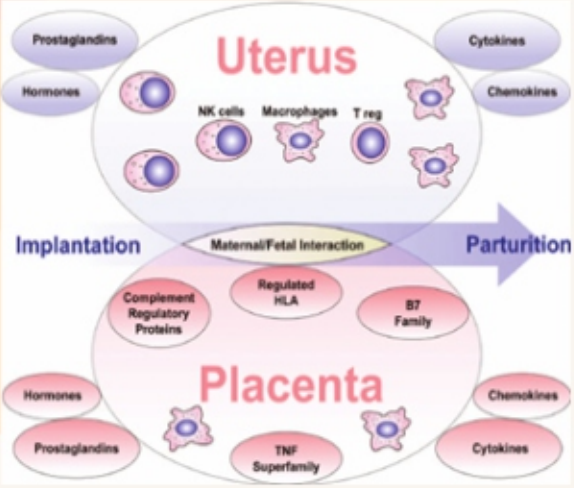
Maternal Immune Adaptations

- In healthy pregnancy, however, the foetus is not compromised by an allogenic immune response.
- In these pregnancies, a crosstalk between the pre-embryo and the mother-to-be starts early after fertilization, and results in a protective immune response in the mother.

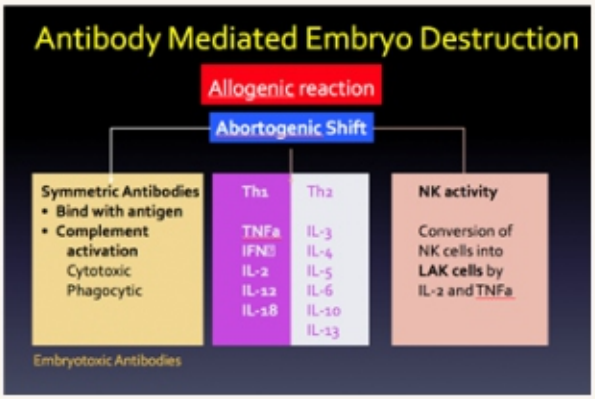
MOGS Prizes - Thesis (Deadline 31st December, 2021)

Sr. No.	Name of the Prize	Criteria	
		Subject	Eligibility
1.	**MOGS Dr. R. D Pandit Essay Competition**	1500 words essay on Topic: "New Vistas in Women's Health"	Senior Category: Age more than 40yrs Junior Category: Age less than or 40 yrs

Note: Kindly send 5 copies of the Essay along with CV and Covering letter. In the covering letter following should be mentioned Mobile number & Email id.



Multiple mechanisms underlie maternal tolerance of the fetus. Mothers, via changes that occur in the uterus, and embryo/fetuses, via special adaptations of the placenta, contribute to the establishment of an immune privileged environment within which the semiallogeneic fetus resides safely until termination. NK cells, natural killer cells; Treg, CD4 □ regulatory T cells; TNF superfamily, tumor necrosis factor superfamily.

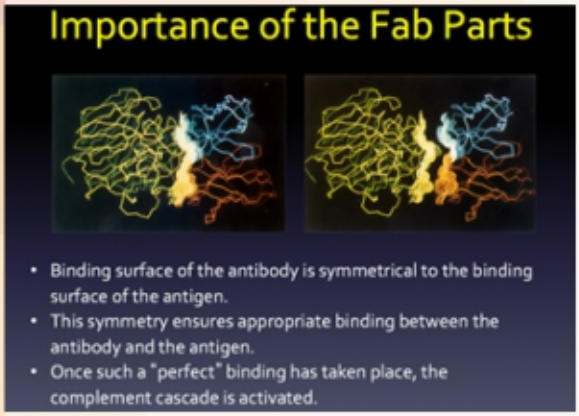


In abortion or embryo destruction due to immunologic interaction, 3 pathways are involved.

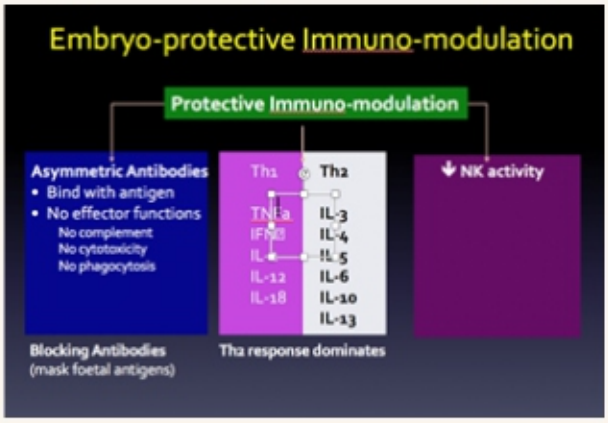
- The symmetric (cytotoxic) antibodies bind with the foetal antigens via the Fab parts. Next, there is activation of the complement cascade at the Fc part of the antibody resulting in cytotoxic and phagocytic

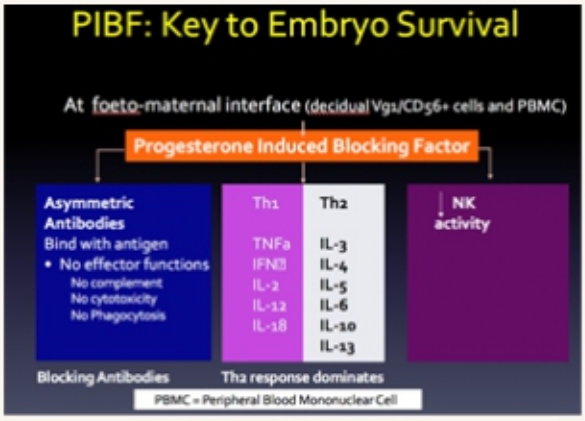
reactions, eventually causing destruction of the foetus.

- The Th1 (T helper cell 1) response dominates, which in contrast to the foeto-protective Th2 (T helper cell 2) response, results in abortion.
- The release of Th1 cytokines, TNF (Tumor Necrosis Factor) and IL-2 (Interleukin-2), convert the NK (Natural Killer) cells into LAK (Lymphokine Activated Killer) cells.



The left image shows the Fab part of the antibody binding to the antigen. The Fab surface of the antibody fits perfectly with the relevant part of the antigen so that the mechanism can be compared to a lock and key. The second image on the right shows a slight separation between the antibody and antigen, so that we can appreciate how exactly their binding surfaces are aligned with one another. In other words, the binding surface of the antibody is symmetrical to the binding surface of the antigen. This symmetry ensures appropriate binding between the antibody and the antigen. Once such a "perfect" binding has taken place, the complement cascade is activated.





Having understood the abortogenic shift, it is now easy to understand the mechanisms in favor of embryo protection - exactly the opposite mechanisms to those for embryo rejection.

Embryo-protective immuno-modulation takes place in 3 ways:

1. The antibodies are asymmetric. As a result, they do not bind perfectly with the antigens, but only block the

The key to this embryo-protective immuno-modulation and embryo survival is Progesterone Induced Blocking Factor, or PIBF.

· PIBF is produced by CD56+ cells at the foeto-maternal interface.

· PIBF induces asymmetric antibodies, Th2 response and reduces NK cell activity.

· In this way, PIBF ensures embryo-protective immuno-modulation.

antigenic structures without subsequent activation of the complement cascade and cytotoxic and phagocytic reactions.

2. The protective or favorable Th2 response dominates, resulting in activation of protective cytokines, with suppression of the harmful Th1 response.

3. There is no TNF and Interleukin 2 release. Therefore, the NK cell activity diminishes and there is no conversion of NK cells to embryotoxic LAK cells.

This events sequence constitutes a protective immuno-modulation.

(Note: V1 are a histochemically well described cell population.
PBMC stands for Peripheral Blood Mononuclear Cells)

Benefits of Progesterone : Evidenced Based Medicine

- American Journal of Obstetrics & Gynecology (1994)
- Progesterone supplementation increased leukocyte and T cell concentration in human endometrium
- Journal Gynaeol Obstetrics Biological Reproduction (2004)
- Progesterone supplementation exerts a pregnancy protective effect by induction of Th2 based immunoprotective response
- Reprod Biomed Online (2006)
- Progesterone probably acts as an immunological suppressant blocking T – helper (Th) 1 activity and inducing release of Th2 cytokines

Two way Immunomodulation:

- Dydrogesterone induces PIBF thereby upregulates Th2 cytokines, asymmetric antibodies, NK cells.
- Dydrogesterone directly upregulates Th2 cytokines and downregulates Th1 cytokines

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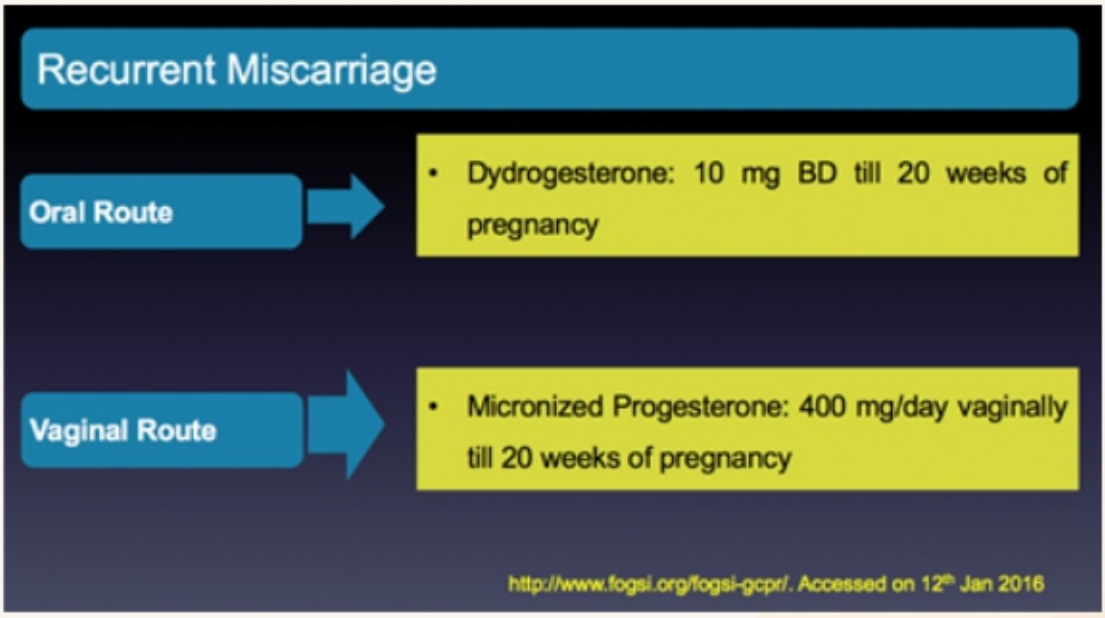
FOGSI Position Statement 2015



Conclusion

- Recurrent pregnancy loss is a vexing problem facing many couples.
- Some authors have suggested that idiopathic recurrent pregnancy loss is alloimmune in nature.
- Suggested mechanisms include the presence of cytotoxic antibodies, absence of maternal blocking antibodies, inappropriate sharing of human leukocyte antigens, and disturbances in natural killer cell function and distribution.
- Proposed therapies for so-called alloimmune-related pregnancy loss include leukocyte immunization and intravenous immune globulin. Unfortunately, neither has been successful in well-designed trials and both are expensive.
- Progesterone is an essential hormone in pregnancy which is widely used in the management of threatened miscarriage, recurrent miscarriage, and preterm labour.
- Progesterone acts via PIBF on the endometrium exerting immunomodulatory and anti-inflammatory action ensuring the maintenance of pregnancy.
- Supplementation with progesterone exhibits a positive benefit–risk profile by improving live birth rates in women with RPL.

Genetics and Recurrent Pregnancy Loss


Dr. Punit Bhojani


Ms. Shivanjali Kapse-Jadhav


Dr. Chaitanya Datar


Dr. Tejal Poddar

Genetic causes are the most common entities resulting in first trimester abortion. The frequency of aneuploidy is almost 90% in fetal loss in the first 6 weeks; about 50% in losses 8 to 11 weeks of gestation; 30% in those with 16-19 weeks and less than 10% above 20 weeks. (These numbers look very high please quote reference)

Gestational age	Risk of miscarriage
At conception	75%
Visible gestational sac	10-15%
FHS detected- 6 weeks	9.4%
7 weeks	4.2%
8 weeks	1.8%
9 weeks	0.5%
12 weeks	0.5%
Second trimester	3%
Third trimester	1%

Genetic causes for RPL include-

- Chromosomal Factors
- Single gene (rare) abnormalities causing- Recurring IUDs or anomalies
- Thrombophilias
- Metabolic Factors eg- MTHFR deficiency causing hyoerhomocysteinemia

GENETIC FACTORS AS THE CAUSE OF RPL

There are a variety of genetic factors that may result in failure of a pregnancy to develop. These include aneuploidy, chromosomal imbalances as a result of parentally harbored translocations or inversions, deletions or duplications of genetic information within chromosomes, and single-gene mutations

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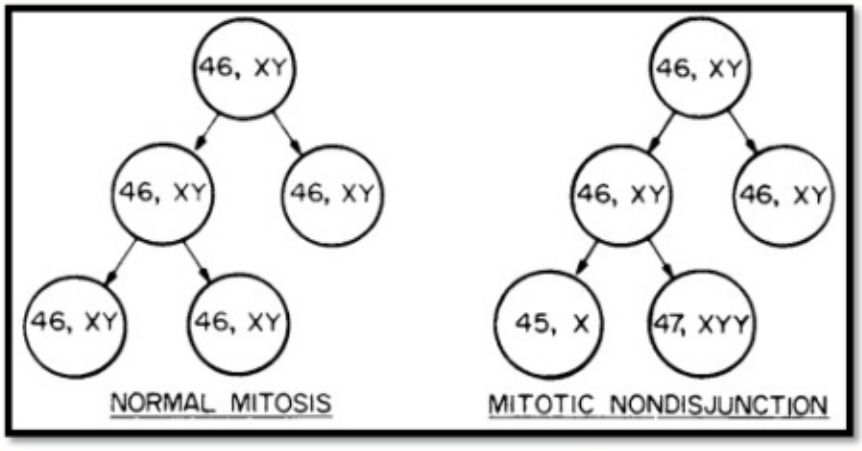
Chromosomal findings in RPL

Apparently normal	40%
Abnormal	60%
•Trisomy (47 chromosomes – 1extra)	30%
•45X (45 chromosomes – one missing)	10%
•Triploidy (69 chromosomes – three sets)	10%
•Tetraploidy (92 chromosomes – four sets)	5%
•Other chromosome anomalies (e.g. structural anomalies)	5%

Broadly, genetic factors may be divided into embryonic errors derived from known parental genetic abnormalities and embryonic errors that arise de novo in apparently genetically normal parents

Chromosomal abnormalities like aneuploidy or polyploidy result from random errors in germ cell development that affect s pregnancies in couples with and without a history of RPL equally. Typically, numerical aneuploidy results from meiotic nondisjunction in the germ cells of couples with normal parental karyotypes, and the recurrence of a particular abnormality in future pregnancies is rare



Structural chromosomal abnormalities:

Parental structural chromosomal anomalies are present in 3-5% of couples with RPL as compared to 0.7% in the general population.

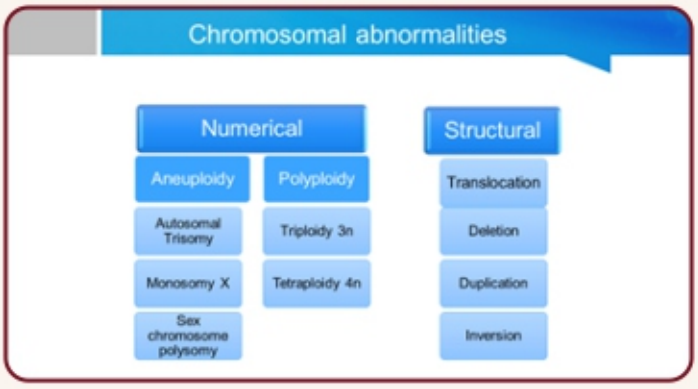
Balanced translocations are the most common chromosomal abnormalities contributing to RPL. In couples with RPL, this abnormality is found more frequently in the female partner at a ratio of 2:1 up to 3:1. Recent data from PGT (PGT-A) has shown that embryos resulting from parents harboring a balanced reciprocal translocation have rates of unrelated chromosomal aneuploidy exceeding 35%. Studies indicate that when the Robertsonian translocation is maternal, there is a greater risk that the fetus will exhibit an unbalanced genotype and phenotype.

All balanced translocations can be detected by ordering a peripheral karyotyping in parents. Parents carrying balanced translocations are usually asymptomatic.

Pregnancies with unbalanced translocations usually end in miscarriage – which is often seen as a natural selection mechanism – but can also lead to intra uterine fetal deaths (IUFD), or even live births with major congenital defects.

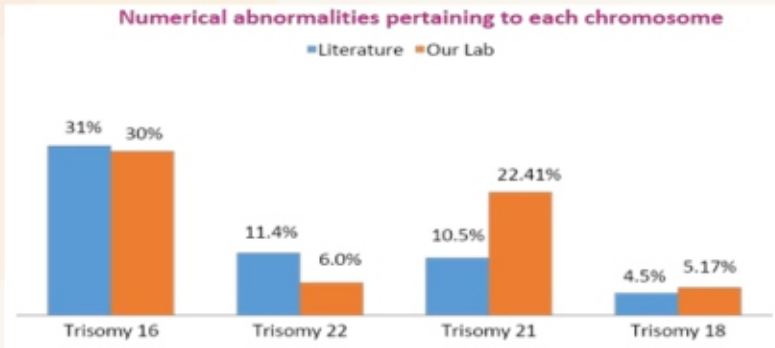
In males, carrier of balance translocations usually have concerns pertaining to fertility because of the arrest of spermatogenesis ensuring in poor semen quality and quantity.

Inversions in the chromosomes need to be studied well, as inversions would lead to chromosomal loss or gain at the breakpoints.



Numerical chromosomal abnormalities:
Numerical abnormalities are a type of chromosomal defect. These types of birth defects occur when there is a different number of chromosomes in the cells of the body from what is usually found. So, instead of the typical 46 chromosomes in each cell of the body, there may be 45 or 47 chromosomes.
Common types of numerical aberrations are: triploidy, trisomy, monosomy and mosaicism.

Few chromosomes are highly involved in causing RPL- like chromosome 16, 18, 21, 22.

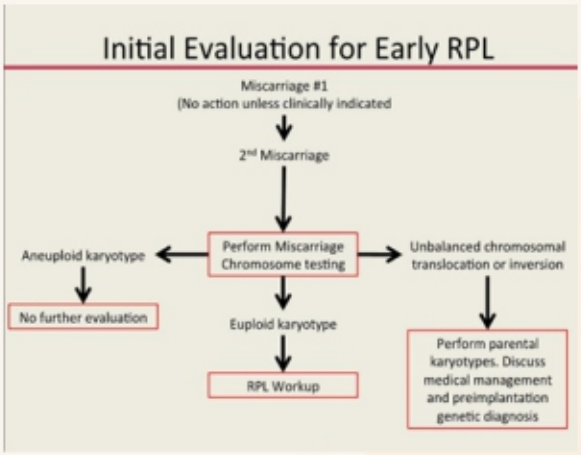


Which test to choose when?

Advantage of Microarray over Karyotype for specimen type- product of conceptus.

INVESTIGATION/LAB EVALUATION

Conventional Karyotyping	Chromosomal Microarrays
Involves cell culturing	No cell culture required
Challenges with culturing in some samples	Higher Success rate
Detects only large chromosomal re-arrangements, (resolution 5-10Mb)	Detects sub-microscopic chromosomal re-arrangements (resolution depending on array)
Sample collection more tedious	Easy sample collection
Cannot rule out maternal contamination	Maternal cell contamination testing done on all Prenatal samples
Can pick up balanced translocations and inversions	Cannot pick up balanced translocations (not cause of abortion)



- Couple Karyotype should be done in
  - ✔ Repetitive first trimester losses
  - ✔ Anembryonic pregnancy
  - ✔ History of congenital malformations or intellectual disability in previous pregnancy

Knowledge of the chromosomes of the products of conception allows an informed prognosis for a future pregnancy outcome. If the karyotype of the miscarried pregnancy is abnormal, there is a better prognosis for the next pregnancy.

Detection of numerical error in chromosomes entails no further testing or treatment, since:
1) It is mostly non-recurrent
2) The risk of another miscarriage is not increased above that of any woman of the same age.
The triad of analysis includes the POC testing by microarray and karyotype of both the parents.

Significance of Chromosome Testing of Embryonic Material/ parental blood: Miscarriage tissues provide a rich source of material to determine the origin of chromosome errors. The opportunity can be utilised only if counselling is done in advance and the parents are explained about the need for the tissue analysis. This is because the products of conception may be minimal and there is a need to send with appropriate precision for analysis.

Methods used to analyze can be broadly classified into

- Chromosomal abnormalities-

1. Fluorescence in situ hybridization (FISH)
2. Conventional karyotyping
3. Chromosomal Microarray comparative genomic hybridization

- Gene level abnormalities-

1. Quantitative fluorescence polymerase chain reaction (Qf-PCR).
2. Multiple ligation dependent probe amplification (MLPA)
3. Exome based testing – Whole exome/ Clinical exome.

Testing: Whole karyotype may be difficult in Product of conceptus (POC) cases- success rate variable- 20-40%

Importance of Genetic Counselling-

Genetic counselling is important for

1. To understand the family history by taking a complete three generation pedigree.
2. Understand the cause for RPL.
3. Discuss the appropriate testing options to be able to reach a diagnosis in cases of RPL.
4. To understand the genetic results, its significance and further work up in other family members.
5. After the cause of RPL is diagnosed and it suggests a genetic aetiology- further options of pre-conceptional and prenatal testing must be discussed. Diagnosis of RPL.

Management options-

· Reproductive options need to be discussed in couples with chromosomal aberrations and these may include natural conception with prenatal diagnosis, gamete donation and adoption.

· Pre-implantation genetic testing (PGT), PGT has been proposed as a treatment option for translocation carriers. Since it necessitates IVF, couples with proven fertility need to be aware of the financial cost as well as implantation and live birth rates per cycle.

MOGS Scholarships - (Deadline 31st December, 2021)

Sr. No.	Name of the Prize	Criteria	
		Subject	Eligibility
1.	**MOGS- Dr. Shantabai Gulabchand Travelling Fellowship Award**	Training abroad in specialized areas in OBGYN	Age not be more than 35 years, Life member of the Society or an ordinary Member for at least the last 5 continuous years Post graduate qualification in the subject of Obstetrics & Gynecology
2.	**MOGS Dr Bhanuben M Nanavati Scholarship for Overseas Studies**	Training abroad in specialized areas in OBGYN	MOGS member for 3 years, Age less than 40 years, Not received the award earlier, Well acquainted with the subject and country of study
3.	**MOGS Dr C G Saraiya Traveling Fellowship**	Training in India in specialized areas in OBGYN	Postgraduate qualification, Age less than 40 years

Endocrinological Perspectives in RPL

Dr Pratik Tambe MD FICOG
Chairperson, AMOGS Endocrinology Committee (2020-22)
Governing Council member, ICOG (2021-22)
Chairperson, FOGSI Endocrinology Committee (2017-19)
Managing Council member, MOGS, MSR and ISAR
drpratiktambe@gmail.com

Background

Implantation and maintenance of pregnancy is a synchronised balance among various endocrinological, immunological, genetic, anatomical and environmental factors. Approximately 8-15 % of all pregnancy losses and recurrent pregnancy losses are due to endocrine factors. Hence, endocrine abnormalities need to be evaluated in patients with history of recurrent pregnancy loss. Diagnosis and treatment of these endocrine abnormalities can help in improving both the maternal and fetal outcomes.

The major endocrinological causes of recurrent pregnancy loss (RPL) are:

- Thyroid dysfunction
- Polycystic ovaries
- Obesity
- Hyperinsulinaemia & insulin resistance
- Hypersecretion of LH
- Hyperandrogenemia
- Hyperhomocysteinemia
- Hyperprolactinaemia
- Luteal phase deficiency
- Low serum hCG levels

Thyroid dysfunction

Thyroid disease is one of the most common endocrine abnormalities seen in pregnant women. It affects 2 - 5 % of pregnant women and is associated with adverse pregnancy outcomes.

Impact of maternal dietary iodine deficiency

- Impaired maternal and fetal thyroid hormone synthesis
- Increased maternal pituitary TSH production
- Maternal and fetal goitre
- Increased rates of pregnancy loss, stillbirth
- Increased perinatal and infant mortality

Thyroid hormone and fetal neurology

- Essential for neuronal migration
- Myelination
- Structural changes in the fetal brain

- Adverse effects on the cognitive function
- Cretinism and profound intellectual impairment
- Deaf mutism
- Motor rigidity

Iodine deficiency is the leading cause of preventable intellectual deficits worldwide.

Normal levels during pregnancy

The recommended upper TSH value in the first trimester in both the 2011 and 2012 ATA (American Thyroid Association) guidelines is 2.50 mIU/L and 3.00 mIU/L in the second and the third trimester. The ITS FOGSI Guidelines on Thyroid Dysfunction published 2019 also echo the same cut offs.

Anti-TPO antibodies

As regards the incidence of TgAb and TPOAb in patients with recurrent losses, some studies report a higher incidence while others demonstrated no difference when compared to healthy controls. A meta-analysis of eight studies that included 460 Ab-positive patients and 1,923 controls noted a significant association between thyroid Ab positivity and recurrent pregnancy loss (OR 2.3 95% CI 1.5–3.5).

The data for an association between thyroid antibodies and recurrent pregnancy loss is less robust than for sporadic loss. Some studies have reported that women with recurrent pregnancy loss who were antithyroid Ab positive also demonstrated higher levels of anticardiolipin Ab and other non–organ-specific antibodies.

Overt hypothyroidism

Maternal hypothyroidism is the most frequent endocrine disorder in pregnancy, associated with a number of adverse pregnancy complications as well as detrimental fetal effects. Treatment with levothyroxine is indicated to prevent the adverse complications and improve the pregnancy outcome.

Subclinical hypothyroidism

Subclinical hypothyroidism (SCH) is defined as an elevated TSH concentration with concurrent normal thyroid hormone concentrations. It is estimated to affect upto 2–3% of all pregnancies.

Levothyroxine treatment in women with RPL and SCH is controversial. A reduced risk of pregnancy loss was seen with levothyroxine treatment in a retrospective analysis of 5,405 pregnant women with SCH. Hence, the benefits of treatment need to be weighed against the risks.

The European Thyroid Association Guidelines state that SCH arising before conception or during gestation should be treated with levothyroxine. The ATA also recommends levothyroxine treatment for pregnant women with SCH (with TSH above trimester specific ranges) and TPO-Ab, or SCH (with TSH above 10 mIU/L).

Hyperthyroidism

The prevalence of overt hyperthyroidism in pregnancy is about 0.2–0.4% and that of subclinical hyperthyroidism in pregnancy is about 1.7–2%. Overt hyperthyroidism (most commonly caused by Graves' Disease) is associated with higher frequency of pregnancy complications. According to the Endocrine Society Clinical Practice Guideline (ESCPG) and the ATA, hyperthyroidism needs to be treated with anti-thyroid drugs propylthiouracil (PTU) or methimazole (MMI).

Thyroid autoimmunity

This is the presence of thyroid antibodies against thyroid peroxidase (TPO-Ab) and/or thyroglobulin (Tg-Ab) in combination with a normal or abnormal thyroid function. It has an incidence of 8-14% among women of reproductive age group. Greater risk of miscarriage associated with thyroid autoimmunity could be due to the increased auto-immune imbalance that leads to a greater rejection of the fetal graft.

It is recommended to perform thyroid screening (TSH and TPO-Ab) in women with RPL. If hypothyroidism is present, it should be treated with levothyroxine. But, if patient is euthyroid, then levothyroxine treatment to improve the pregnancy outcomes is still controversial.

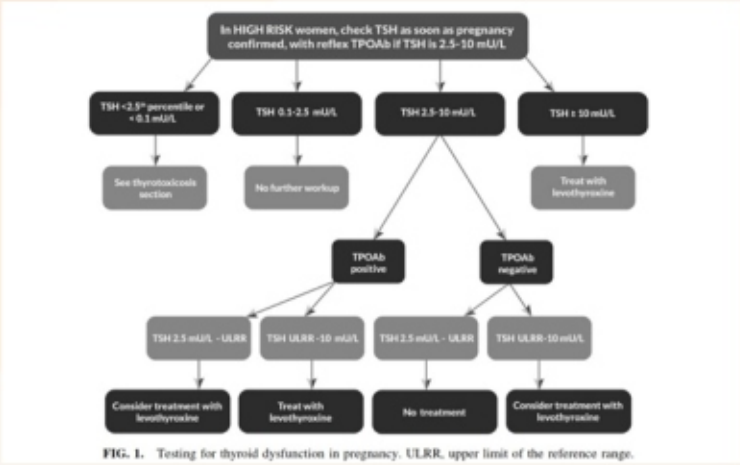


FIG. 1. Testing for thyroid dysfunction in pregnancy. ULRR, upper limit of the reference range.

Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility and a common abnormality among women with RPL. Spontaneous and recurrent pregnancy loss occurs in 40% of women with PCOS23 mainly due to the various metabolic associations of PCOS.

Obesity

Obesity has various detrimental effects on the female reproductive function through hyperinsulinaemia and hyperandrogenemia. Maternal obesity with BMI > 30 kg/m2 has been reported as an independent risk factor for euploid miscarriage. Insulin resistance is the main linking factor among obesity, PCOS and RPL.

Hyperinsulinaemia and insulin resistance

Insulin resistance (IR) is an independent risk factor for early pregnancy loss in women with or without PCOS. IR and subsequent hyperinsulinaemia is the common linking factor in the pathophysiology of miscarriage in PCOS.

Mechanisms of RPL in PCOS

- Effect on oocyte maturation
- Glucose uptake and metabolism
- Impaired implantation
- Altered expression of HOXA10 gene
- Reduction of serum glycodelin (inhibits endometrial immune response)

- Reduced insulin like growth factor binding protein-1 (IGFBP-1) (facilitates embryo adhesion)
- Increased level of PAI-1 induces a hypo-fibrinolytic state
- Villous thrombosis leads to trophoblastic hypoplasia and miscarriage
- Hypersecretion of LH is associated with premature oocyte aging and poor endometrial development.
- Hyperandrogenemia regulates uterine receptivity by downregulating the HOXA10 gene
- Reduced concentration of glycodelin A in the peri-implantation period

Hyperhomocysteinaemia

Hyperhomocysteinemia is a risk factor for venous thrombo-embolism and is associated with neural tube defects, pre-eclampsia, placental abruption and RPL as per a meta-analysis. Recent studies have reported conflicting results.

RPL affected PCOS patients seemed to have an increased incidence of hyperhomocystinemia compared to women with RPL without PCOS. There is increased microthrombi formation in the placental bed leading to poor placentation.

Various studies have reported the role of folic acid, vitamin B6, vitamin B12 and low molecular weight heparin (LMWH) in improving the pregnancy outcomes in women with hyperhomocysteinemia.

Hyperprolactinemia

Hyperprolactinemia is associated with miscarriage, especially in women who have experienced unexplained RPL.

Luteal Phase Deficiency

LPD is a condition wherein there is insufficient progesterone exposure to maintain a regular secretory endometrium to allow for normal embryo implantation and growth. LPD can be caused by several endocrinopathies, including stress, PCOS and prolactin disorders. Studies have failed to confirm a strong association between LPD and RPL. Hence, LPD testing is not routinely recommended.

Progesterone production triggers favourable morphological and physiological changes in the endometrium creating a suitable environment for the embryo during the implantation window. Progesterone maintains pregnancy by

downregulation of Th1 cytokines and stimulation of Th2 cytokines.

The PROMISE Trial showed that progesterone therapy in the first trimester of pregnancy did not result in a significantly higher rate of live births (65.8% vs 63.3%),50 but there has been criticism of the trial regarding the dosage of progesterone therapy used during the trial.

The most recent Cochrane meta-analysis published October 2018 considered 13 trials with 2,556 women and concluded that progesterone supplementation probably reduces the number of miscarriages compared to placebo (RR 0.69). There is a slight benefit as regards improved live birth rate (RR 1.11), reduction of preterm births (RR 0.59) and a possible reduction in stillbirths (RR 0.38).

Conclusions

Factors responsible for RPL are multiple and endocrine dysfunction is one of them. Altered endocrine profile results in pregnancy losses in the early stages of gestation. There is no strong evidence to support routine testing of LH, androgens, homocysteine or prolactin in RPL. Similarly, there is no evidence to support routine metformin therapy for IR with RPL. Future developments in diagnosis and evidence of efficacy of treatment of endocrine disorders among patients with RPL are much awaited, for the ultimate goal of any clinician is not just to aim at successful implantation but a successful pregnancy outcome.

Forthcoming Events

12th December, 2021
MOGS Dr. B N Purandare Clinical Activity on
New Vistas in Gynecological Oncology"

05th February, 2022
MOGS Youngistan Conference

26th & 27th February, 2022
Golden Jubilee Annual Conference of MOGS

23rd to 27th March, 2022
MOGS Dr. Nandita Palshetkar PG Crash Course CME- 2022

Anatomical Causes of Recurrent Pregnancy Loss

Dr Sanket Pisat
Gyn Endoscopic surgeon Mumbai
Member MC MOGS and IAGE

Dr Mansi Medhekar
Consultant Obstetrician and Gynaecologist
Member of Managing council MOGS

Dr Medha Tankhiwale
Consulting Obstetrician & Gynecologist
Member of Youth Council MOGS

Recurrent pregnancy loss is defined as having 3 or more consecutive pregnancy losses prior to 20 weeks of gestation. It encompasses a wide spectrum of causes, of which, 15% can be attributed to anatomical causes. These include preexisting uterine anomalies or abnormalities in the uterus secondary to surgical procedures such as curettage or cervical dilatation. All of the can be easily diagnosed and effectively treated so as to significantly improve the reproductive outcome.

SEPTUM

DIAGNOSIS	SYMPTOMS	CONFIRMATION	TREATMENT
1. USG: Two Cavities **2. HSG:** Two separated cavities with indentation at the fundus	Non specific	**A. 3D USG:** **<Image 1>** Internal indentation >50 % of the uterine wall thickness **(CONUTA CLASSIFICATION)** No fundal indentation of the outer contour **B. HYSTEROSCOPY AND LAPAROSCOPY:** Indentation on Hysteroscopy between Ostia but No Fundal indentation on laparoscopy Not possible to diagnose on Hysteroscopy alone D/D: Bicornuate Uterus	**INDICATIONS FOR SURGERY:** 1. Recurrent 1st Trimester abortions (with other causes ruled out) 2.Infertility Although there is conflicting evidence in literature SURGERY: Septal incision with cold scissors, end point of which is to achieve a slightly arcuate uterus (not completely flat)

INTRAUTERINE SYNECHIAE

1. HSG: Irregular filling defect in the cavity Irregular T shaped Uterus Fundal Indentation Irregular/ Assymetrical **2. USG :** Thin Endometrium Cystic Fluid filled Spaces at the Fundus	1.Hypomenorrhea/ Amennorhea 2.Previous history of Obstetric Curettage /MTP Past History of Pelvic tuberculosis	HSG is confirmatory 3D USG to identify extent and grade and to rule out other anomalies Hysteroscopy -Cervical Stenosis is common Narrow cavity with minimum endometrium Bands of fibrosis Between Anterior and Posterior wall	**INDICATION:** Any confirmed case of synechiae requires surgery **SURGICAL TECHNIQUE :** Division of Surgical Bands with scissors. Division of lateral and fundal adhesions with hysteroscopic scissors to restore normal shape of cavity

T SHAPED UTERUS

1. HSG: Small T shaped cavity with reduced uterine volume **2. USG 2D:** Thinning out of Endometrium in lower half /lower 2/3rds of cavity in saggital view	Recurrent second trimester miscarriages Subfertility	**A. 3D USG (CUME CRITERIA)** <Image 2> Interpretation of CUME CRITERIA: 1.All three resent: T Shaped Uterus 2.Only 2 out of 3 present:Borderline T shaped Uterus3.Only one present: Normal Uterus **B. HYSTEROSCOPY:** Visualisation of small cavity Non Visualisation of tubal ostia from the level on the internal os Laparoscopy not required to confirm	INDICATIONS: Recurrent pregnancy loss (proven benefit) Infertility (emerging evidence in favor of surgery) SURGICAL TECHNIQUE : Incision of lateral wall with cold scissors/ Resectoscope till ostia are seen from the level of the internal os

POST OPERATIVE CARE

Adhesion Prevention by intrauterine Pediatric Foleys in case of extensive surgery Cyclical Estradiol valerate and progesterone for three cycles

FIBROID	There is not much evidence to suggest the role of Fibroids and Polyps in Recurrent pregnancy losses hence their treatment may not be justified
POLYP	

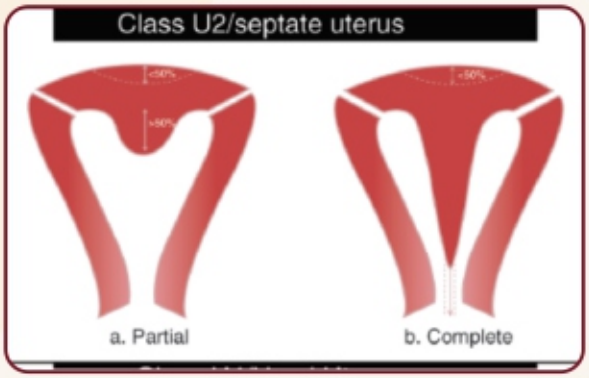


Image 1: Copied from Gynecol Surg (2013) The ESHRE–ESGE consensus on the classification of female genital tract congenital anomalies.

Class U2: internal indentation >50 % of the uterine wall thickness & external contour straight

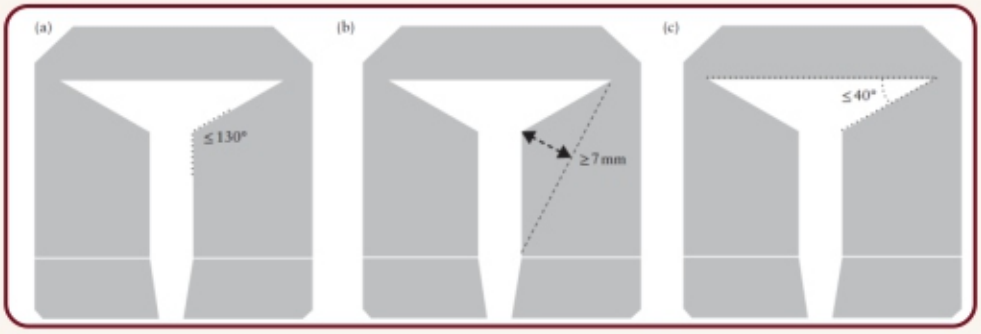


Image 2: Copied from Ultrasound Obstet and Gynecol: CUME criteria for diagnosis of T shaped Uterus T-shaped uterus as defined by CUME (Congenital uterine malformation by experts), according to presence of three criteria beyond particular cut-offs: (a) lateral indentation angle ≤130□, (b) lateral indentation depth ≥7mm and (c) T-angle ≤40□. Presence of two of these three criteria is defined as borderline T-shaped uterus, whereas lack or presence of only one of these criteria is defined as normal uterus with respect to lateral uterine morphology. This definition is supported by reliability and diagnostic accuracy testing of measurements, and by post-test probability >90% for target population, considering diagnosis made most often by experts as reference (i.e. CUME).

Once identified as a case of Recurrent pregnancy loss, it is imperative to investigate for all the aforementioned anatomical causes as they can be easily treated with proven benefits. The initial screening should include – a 2D/3D Ultrasound, Sonohysterography and a Hysterosalpingography. However definitive diagnosis can be achieved by combining laparoscopy and hysteroscopy which can provide, additionally, at the same sitting therapeutic benefits as well. Patients diagnosed with Mullerian Anomalies must be subjected to additional anatomical evaluation of the urinary tract. An MRI may also be offered as an advanced imaging modality, however its benefit in providing additional information is limited. In cases with suspected cervical incompetence, a transvaginal USG can be used to monitor cervical length.

After a diagnosis has been established, it must be determined whether or not the existing anatomical cause mandates treatment, a decision that must be taken in accordance with the current literature. Case studies suggest that Hysteroscopic septum resection improves live birth rates, however, there are no randomized control trials to support this at present. In patients diagnosed with Uterine Septa, Submucosal fibroids, Endometrial polyp and uterine synechiae, the decision whether to treat or not should be individualized. In cases of cervical incompetence, prophylactic cerclage must be offered to those with a cervical length of less than 24 mm detected prior to 24 weeks of gestation. There is currently no evidence to show that treatment of Mullerian anomalies) and subserosal/ intramural fibroids offers any benefit to patients of recurrent pregnancy losses

Report of Hybrid MOGS – AMOGS Conference on New Vistas in Fertility Management

held on October 16 & 17, 2021 Saturday & Sunday

Dr. Sujata Dalvi
Joint Clinical Secretary

New vistas in fertility management was held as a hybrid conference. This was a collaboration between AMOGS & MOGS. Dr. Nandita Palshetkar, President AMOGS & Past President MOGS Delivered the oration.

Conveners were Dr. Sujata Dalvi, Dr. Kedar Ganla, Dr. Ameya Purandare, Dr. Pratik Tambe & Dr. Rohan Palshetkar

The program started with Free Paper session in 2 Halls, Dr R D Pandit and Dr M N Parikh Hall. There were 17 free papers – Prizes were given to Best 3 papers separately in both the Halls.

This was followed by Pecha Kucha session to promote young talent. The program was going on simultaneously in both the halls. In Dr R D Pandit hall – Talks on Basic Infertility Management, USG in clinical practice, Ovarian Stimulation Methodologies. In Dr M N Parikh Hall – Talks on Investigations in Infertility, Role of Hystero-laparoscopy, Embryology.

This was followed by On-line and Physical session at Hotel Lalit, Sahar Airport, Andheri, Mumbai. Skit on 'New Vistas in Fertility Mismanagement' was presented by Dr Kedar Ganla and Dr Sanket Pisat. Other participants were Dr Mansi Medhekar, Dr Suman Bijlani and Dr Suchita Pisat. This was followed by Keynote addresed by Dr Hrishikesh Pai – Incoming FOGSI President, Dr Jaydeep Tank, Past FOGSI Secretary and Dr Sunita Tandulwadkar from Poona. Inauguration was conducted by Dr Pratik Tambe and Dr Rohan Palshetkar. Dr Suvarna Khadilkar, Secretary MOGS gave welcome address Dr Sarita Bhalerao gave MOGS President's address. AMOGS President Dr Nandita Palshetkar gave President's address. Introduction of Chief guest, Dr C N Purandare was done by Incoming President MOGS Dr Niranjan Chavan. Dr C N Purandare gave his encouraging speech. Dr Sujata Dalvi, one of the Conveners introduced Guest of Honor, FOGSI President Dr S Shantha Kumari. In her wisdom speech, she

congratulated concerned team for scientific deliberation and thanked all for attending the same. Tribute was given to Dr M N Parikh, whom we lost on October, by Dr Ameya Purandare, Incoming second VP of AMOGS. This was followed by Vote of Thanks by Dr Pratik Tambe. Those present for Physical meet had sumptuous dinner.

October 17, 2021 - Sunday The evening program was courtsy educational grant from Emcure Pharma

The conference started in both Halls simultaneously. Dr R D Pandit Hall, Recurrent Implantation Failure, Expert's Opinion (Seniors with vast experience shared their knowledge) and Cutting Edge Advances – AICC RCOG Session was discussed. Dr M N Parikh Hall, Embryology Lab Improvements, Key Practice Points (Experienced Seniors) and PID – Pelvic Inflammatory Disease was discussed. This was followed by session on Pearls of Wisdom by 3 very Senior Faculty in ART (Dr Sadhana Desai, Dr Firuza Parikh, Dr Kamini Rao). Panel Discussion were conducted on Optimizing IUI Results and Management of Thin Endometrium in Enhancing Success in Endometriosis and Maximizing ART Success Rates in Dr M N Parikh Hall.

The Conference concluded with Valedictory session conducted by Dr Pratik Tambe. Dr Sarita Bhalerao gave concluding remarks on behalf of MOGS and Dr Sujata Dalvi on behalf of AMOGS. Dr Suvarna Khadilkar announced Free Paper Prize winners. Dr Shailesh Kore and Dr Ameya Purandare proposed Vote of Thanks.

4 MMC Credit Points / 10 ICOG Points were awarded to all participate

We would like to express our gratitude to Educational Partners – Emcure for Physical Meet, Sun Pharma, Abbott, Zuventus, Eris, Meyer, Torrent, Astra Zeneca, GSK, Ferring, Intas, Blisson, Shield and Nivian. Sincere Thanx to Onference Team provides Web platform.

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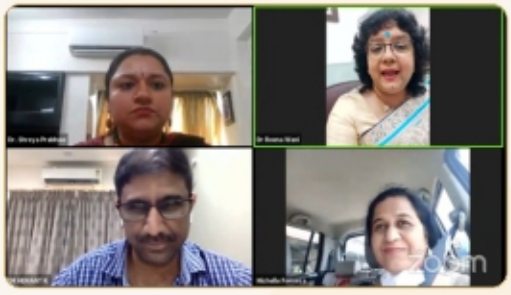
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MOGS PROGRAMS 2021 - 2022

15-8-2021 to 30-11-2021

24.08.2021	MOGS Happy Learning Master Class Webinar Series on Operative Deliveries	Dr. Suvarna Khadilkar, Dr. Komal Chavan Dr. Vandana Bansal, Dr. Gaurav Desai
26.08.2021	MOGS in collaboration with IRC West RCOG Webinar on Vulvovaginal Health	Dr. Sudeshna Ray, Dr. Ashwin Shetty, Dr. Siddesh Iyer
28.08.2021	MOGS Outreach Webinar	Dr. Ameya Purandare,Dr. Priya Vora, Dr. Rohan Palshetkar
29.08.2021	MOGS & SAFOG e cme on New Vistas in Oncology	Dr. Shyam Desai, Dr.Gaurav Desai, Dr.Bhumika Kotecha Mundhe
29.08.2021	MOGS endorsed by World Endometriosis Society international symposium on Revisiting Basic in ART	Dr. Rishma Pai, Dr. Unnati Mamtora, Dr. Sheetal Sawankar
29.08.2021	MOGS CME on Emcure Gynecology Connect	Dr. Jaydeep Tank, Dr. Parikshit Tank
31.08.2021	MOGS E-cme on Managing PPH	Dr. Priti Vyas, Dr. Shreya Prabhoo
05.09.2021	MOGS E CME with Teachers day Felicitation	Dr. Rajendra Nagakatti, Dr. Komal Chavan
23.09.2021	MOGS Outreach program	Dr.Punit Bhojani, Dr. Mansi Medhekar, Dr.Bhumika Kotecha Mundhe
16.10.2021 17.10.2021	MOGS in collaboration with AMOGS E Conf on New Vistas in Fertility Management	Dr. Sujata Dalvi, Dr. Kedar Ganla, Dr.Ameya Purandare, Dr.Pratik Tambe & Dr. Rohan Palshetkar
23.10.2021	MOGS Dr. N.A.Purandare P.G. Teaching Program WITH Mumbai Menopause Society(MMS) hosted by Wadia Hospital	Dr. Geetha Balsarkar, Dr. Sujata Dalvi, Dr.Sunil Tambevekar
24.10.2021	Recent Advances in Obst. & Gyn.	Dr. Punit Bhojani, Dr. Mansi Medhekar, Dr.Bhumika Kotecha Mundhe
31.10.2021	Outreach cme	Dr.Rajendra Nagarkatti,Dr. Sanjay Manjrekar, Dr.Navneet Desai
14/11/2021	Covid 19 Pandemic & PCOS	Dr.Ganpat Sawant, Dr.Parikshit Tank, Dr.Mahduri Mehendale
18/11/2021	MOGS E Outreach program on Vaccination in Pregnancy	Dr.Ganpat Sawant, Dr.Parikshit Tank, Dr.Mahduri Mehendale
20/11/2021	CME ON CURRENT GUIDELINES	Dr. Pratik Tambe, Dr.Priti Vyas
27/11/2021	MOGS Dr. N.A.Purandare P.G. Teaching Program hosted by V. N. Desai Hospital	Dr. Komal Chavan, Dr. Lalita Mayadeo

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Dr Priti Vyas

Dr Dr. Aspi Raimalwala

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- Folivian — Human Follicle Stimulating Hormone Inj. I.P. 75 I.u. / 150 I.u.

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- Progivian — Natural Micronised Progesterone 100 / 50 mg /1 ml. Inj.
- Progivian -AQ — Natural Micronised Progesterone Inj. 50 mg / 1 ml. Inj.
- Progivian — Natural micronised progesterone gel 8% w/w

For Better Implantation

- Lomovian 20 mg — Low Molecular Weight Heparin Inj.
- Lomovian 40 mg — Low Molecular Weight Heparin Inj.
- Lomovian 60 mg — Low Molecular Weight Heparin Inj.
- LomovianMD 300 mg Cartridge — Low Molecular Weight Heparin Inj.
- Atosivian 6.75 mg / 37.5 mg

For Oligohydramnios

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For Better Ovulation Induction

- Letrovian 2.5 mg/5 mg — Letrozole Tablet

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