Indian Fertility Society

Synapse 2nd Edition

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Aim of Synapse

- It provides the content that can be assessed by learners anytime and anywhere.
- During busy practice it becomes difficult to read the whole guidelines, its a ready reckoner or a quick check to know what should be the practice when it concerns recurrent pregnancy loss.
- It includes the delivery of just-in-time information and guidance from experts.
- It provides the information regarding updated guidelines.

Who all are benefited

• Postgraduates • Fellows • Gynaecologists

RECURRENT PREGNANCY LOSS

A pregnancy loss (miscarriage) is defined as the spontaneous demise of a pregnancy before the fetus reaches viability. It includes all pregnancy losses (PLs) from the time of conception until 24 weeks of gestation.[1]

Recurrent pregnancy loss (RPL) is defined as the loss of two or more pregnancies. This definition includes pregnancy losses both after spontaneous conception and ART, but excludes ectopic, molar pregnancies and implantation failure. It describes the cases where all pregnancy losses have been confirmed as intrauterine miscarriages.[1]

PREVALENCE:
It is estimated that fewer than 5% of women will experience two consecutive miscarriages and only 1% experience three or more.

Risk Factors and health behaviour modifications in RPL patients [1,4] (Eshre Guideline update, 2022)

S.No.	Risk Factors	Evidence
1.	**Female age**	The risk of pregnancy loss is lowest in women aged 20 to 35 years and it rapidly increases after 40 years.
2.	**Smoking**	Smoking could have a negative impact on their chances of a live birth, and therefore cessation of smoking is recommended.
3.	**Body Mass Index**	Maternal obesity or being significantly underweight is associated with obstetric complications and could have a negative impact on their chances of a live birth and on their general health. Thus to maintain normal BMI.
4.	**Alcohol**	Excessive alcohol consumption is a possible risk factor for pregnancy loss and proven risk factor for fetal problems (Fetal alcohol syndrome) and therefore limit the alcohol consumption.

Recurrent Pregnancy Loss
Etiology/Investigations/Treatment of Recurrent Pregnancy Loss [1,4]

S.No.	Causative Factor	Recommended Screening	Not Recommended	Treatment
1.	**Cytogenetic**	None[a]	Genetic analysis of pregnancy tissue. Parental Karyotyping	Genetic counseling
2.	**Hereditary Thrombophilia**	None[b]	Factor V Leiden mutation, Prothrombin mutation, MTHFR mutation, Protein C, Protein S Antithrombin deficiency	Antithrombophylaxis not recommended
3.	**Acquired Thrombophilia (Antiphospholipid Syndrome)**	Lupus anticoagulant, Anticardiolipin antibodies (IgG, IgM) β2glycoprotein I antibodies (IgG, IgM)		Low dose ecosprin (75-100mg/day) starting before conception. Prophylactic dose of Heparin (UFH/LMWH) starting on date of positive pregnancy test.
4.	**Metabolic and endocrinologic**	TSH/TPO antibodies, Prolactin[c]	Assessment of PCOS, Ovarian reserve testing, Serum fasting insulin Serum fasting glucose, Luteal phase insufficiency testing, Serum androgens, Serum LH	Levothyroxine for overt hypothyroidism and for subclinical hypothyroidism with positive TPO antibodies.(2) Euthyroid women with thyroid antibodies and RPL should not be treated with levothyroxine. Dopamine agonists for hyperprolactinemia.
5.	**Immunological factor**	Only HLA class II determination (HLA-DRB1*15:01, HLA-DRB1*07 and HLADQB1*05:01/05:2) could be considered in Scandinavian women with secondary RPL after the birth of a boy, for prognostic purposes.)	HLA testing, Cytokine testing, Antinuclear antibodies, Natural Killer cells, Anti HLA antibody	The use of repeated and high doses of Intravenous immunoglobulin (IvIg) very early in pregnancy may improve live birth rate in women with 4 or more unexplained RPL

6.	**Anatomic (Congenital)**	Transvaginal 3D Ultrasound.[4] All women with RPL could have 2D ultrasound to rule out adenomyosis. If mullerian uterine malformations are there: Investigate for kidneys and urinary tract. If tubal patency to be investigated: SHG is preferred over HSG.	Metroplasty for bicornuate uterus. Uterine reconstruction for unicornuate uterus.	Hysteroscopy septal resection for septate uterus as it improves Live birth rate and decrease miscarriage rate.
7	**Anatomic (acquired)**	Transvaginal 3D ultrasound		Insufficient evidence supporting hysteroscopic removal of submucosal / intramural fibroids or endometrial polyps or intrauterine adhesions
8.	**Cervical Insufficiency**	Serial cervical sonographic surveillance is offered to women with a history of second-trimester pregnancy losses PLs and suspected cervical weakness		Cerclage is considered In women with a singleton pregnancy and a history of recurrent second-trimester PL attributable to cervical weakness
9.	**Male Factor**	Sperm DNA fragmentation could be considered for diagnostic purposes. it is recommended to assess lifestyle in the male partner (paternal age, smoking, alcohol consumption, exercise pattern, and body weight)		Modification of lifestyle factors like, avoiding smoking. alcohol, excessive exercise and weight loss.

A. Genetic analysis of pregnancy tissue is not routinely recommended but it could be performed for explanatory purposes like providing the patient with a reason for the pregnancy loss and help to determine whether further investigations or treatments are required). For genetic analysis of the pregnancy tissue, array-CGH is recommended based on a reduced maternal contamination effect. Parental karyotyping can be recommended based on genetic history (like in case of the previous birth of a child with congenital abnormalities, offspring with unbalanced chromosome abnormalities in the family, or detection of a translocation in the pregnancy tissue).

B. Hereditary hemophilia screening is done if there is family history or previous VTE.

C. Serum prolactin testing is considered when there are symptoms of hyperprolactinemia (oligo amenorrhea).

D. If transvaginal 3D ultrasound is not available, MRI is considered.

Unexplained Recurrent Pregnancy Loss (3)

No apparent causative factor is identified in 50% to 75% of couples with RPL. Patients with unexplained RPL to be counseled that the chance for a future successful pregnancy can exceed 50%-60% depending on maternal age and parity.
Vaginal progesterone may improve live birth rate in women with 3 or more pregnancy losses and vaginal blood loss in a subsequent preganancy.[4]

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2. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C etal. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid 2017;27(3):315-390.
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Abbreviations

ART: Artificial Reproductive Techniques
MTHFR: Methylenetetrahydrofolate reductase
UFH: Unfractionated Heparin
LMWH: Low Molecular Weight Heparin
TSH: Thyroid Stimulating Hormone
TPO Ab: Thyroid Peroxidase Antibody
PCOS: Polycystic Ovarian Syndrome
SHG: Sonohysterography
HSG: Hysterosalpingography
VTE: Venous Thromboembolism

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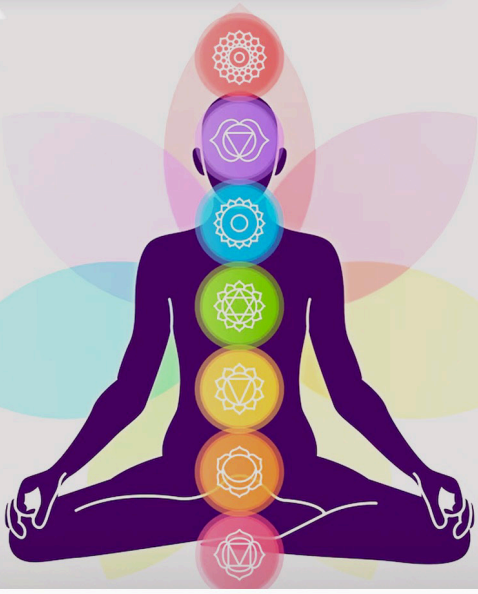

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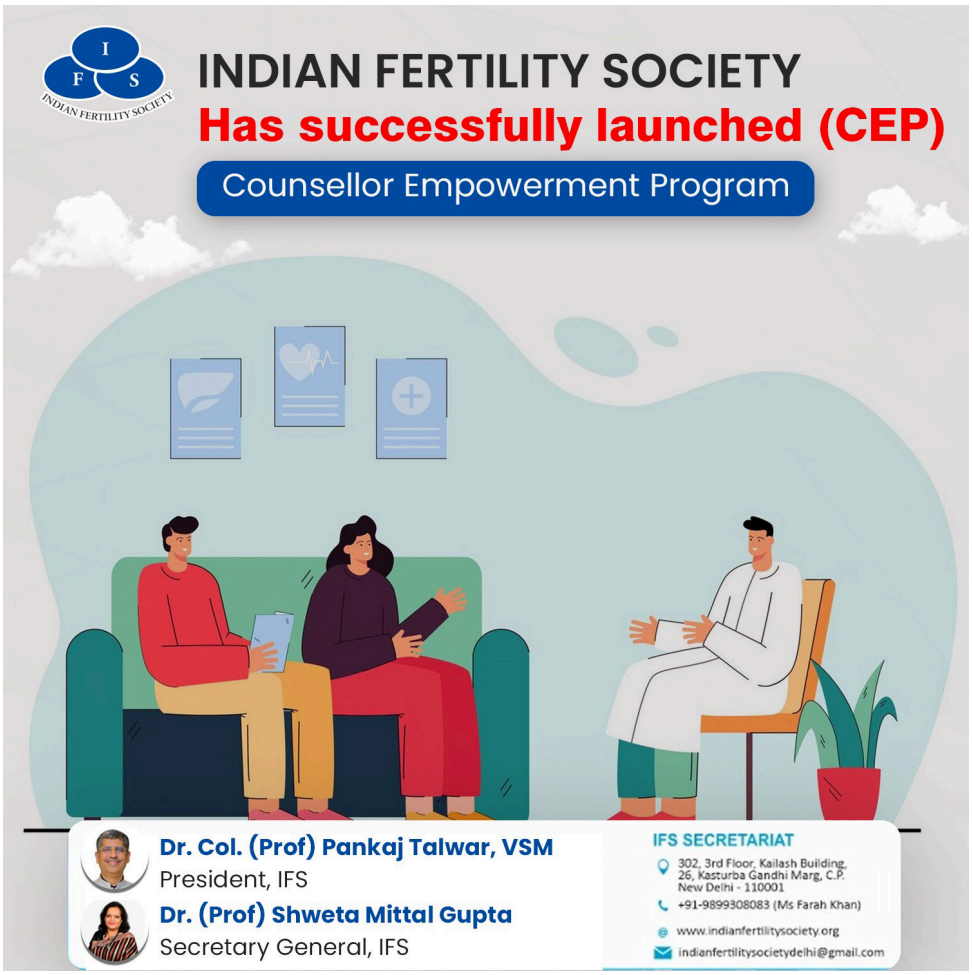
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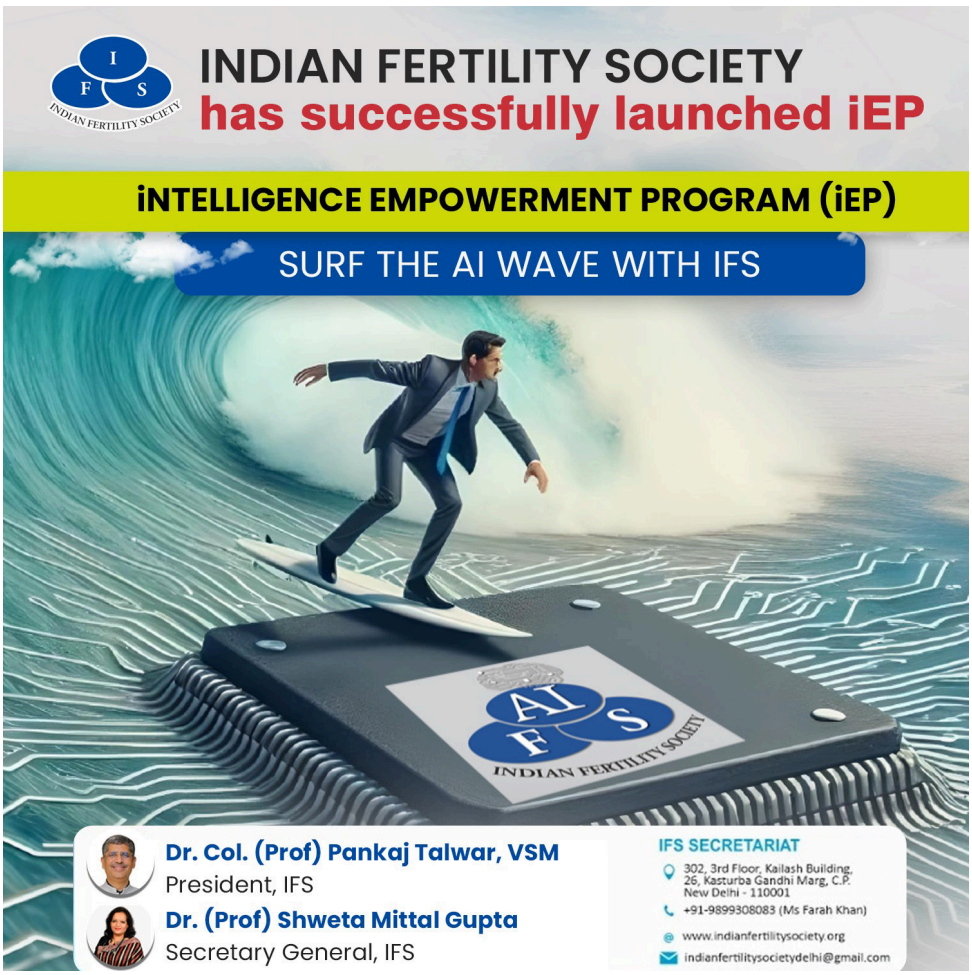
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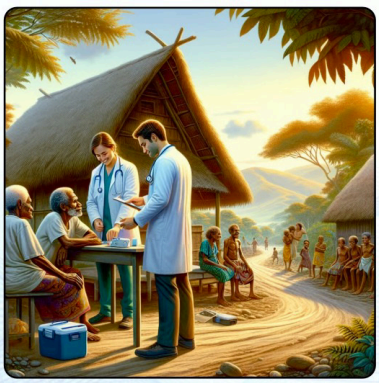

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