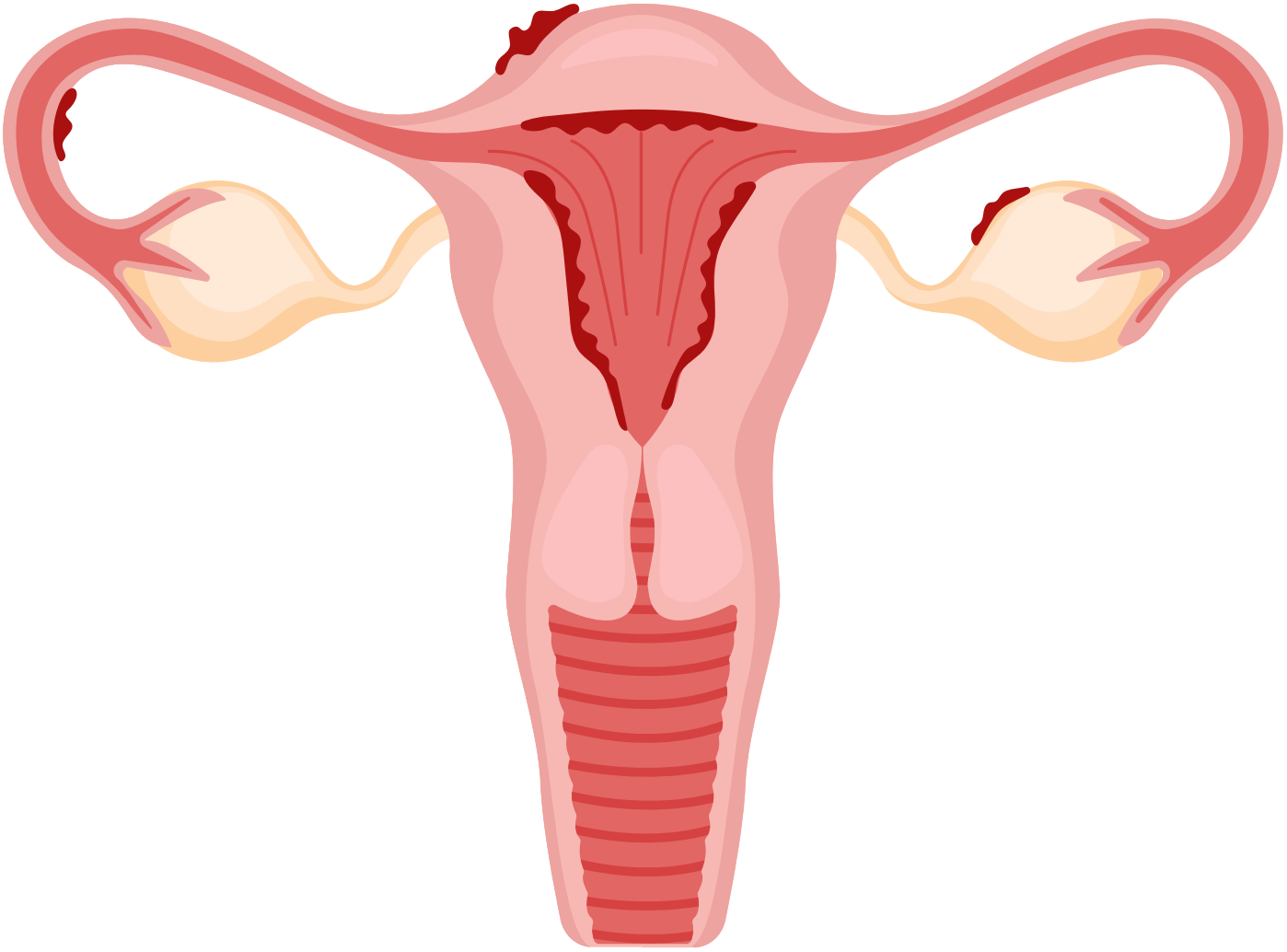
TNFOG

Tamil Nadu Federation of Obstetricians & Gynaecologists



ENDOMETRIOSIS

e News Letter

10th February 2023

PRESIDENT'S MESSAGE

Dear friends,

Greetings to all.

Our TNFOG has started action in full swing, along with routine CMES Bodhana, MARATHON CME & magalir nalam programmes, public awareness activities too. As an initiative, the Mega Cancer screening camp organised at vedasandhur Dindigul has proved the unity of TNFOG & Commitment of our members. Let us move forward to reach the goal of reduction of MMR & Elimination of cancer cervix.

Happy to have the cooperation of all.

Thank you.

Dr. Revathy Janakiraman

President: TNFOG

SECRETARY'S MESSAGE

Dear friends and members of TNFOG,

Warm wishes and hearty greetings of the season to one and all.

After completing our year-round theme-based CMEs on II Friday of every month successfully we are now starting our this year's program on this day, with the theme on Endometriosis.

I congratulate everybody on this happy occasion and thank for their support and cooperation.

This E-Newsletter letter has interesting articles. Go through them during your leisure time and enjoy.

I also have an excellent news to share with you all - our member societies, Madurai and Dindigul OG Societies have won FOGSI National Awards for their Cancer Awareness programs on the World Cancer Day.

Thanks and Congratulations to the members of these societies. I sincerely wish and hope that more societies come forward and take part in such events and win more awards. We have the will and the necessary energy to succeed. Yes, we can do it. Let's do it.

Jai Ho!

Dr. S. Sampathkumari

Secretary: TNFOG

CHIEF GUEST

Dr. Hrishikesh D Pai

President, FOGSI

GUESTS OF HONOR

Dr. Madhuri Patel

Secretary, FOGSI

Dr. Cynthia Alexander

Former Director, IOG

TNFOG MARATHON CME

ON

Endometriosis

Date: 10th February 2023 (Friday) Time: 04:30 PM - 07:30 PM

President

Dr. Revathy Janakiram

Secretary

Dr. S Sampath Kumari

Treasurer

Dr. Vijayalakshmi Gnanasekaran

Chief Guest

Dr. Hrishikesh D Pai
President, FOGSI

Guests of Honor

Dr. Madhuri Patel
Secretary, FOGSI

Dr. Cynthia Alexander
Former Director, IOG

Session 1 - YUVA SESSION

Judges

Dr. Nidhi Sharma
Professor Saveetha Medical College

Dr. Vijayalakshmi Kandasamy
Professor, Chettinad Hospital & Research Institute

Speakers

Dr. Krithiga Meenakshi J
Consultant, OG, Chennai

Dr. Swathisree
Consultant OG Harshitha Hospital, Madurai

Session 2: Scientific Session

Chairpersons

Dr. Banumathy. M
Past President, COGS

Dr. Vani Pujari
Director, Akshaya Women's Centre & Fertility Care

Medical Management of Endometriosis

Dr.Asha Rao
Chairperson,
Endometriosis Committee, FOGSI

Endometriosis and Infertility

Dr. Anu Chawala
Consultant, OG, New Delhi

Session 3: Panel Discussion on Adenomyosis & Infertility

Moderator

Dr. Ramani Devi. T
Past Vice President, FOGSI

Panelists

Dr. Manonmani . R
President, COGS

Dr. Shanthi Rani B
President, Theni OG Society

Dr. Sadhana Devi
Consultant, Gynecologist

Dr. Nirmal Vijayakumar
Consultant,
Queens Fertility Centre

Dr. Rajapriya Ayyappan
Secreatary, IFS TN

Dr. Grace M
President, VOGS

Dr. Radha Madhavi S
Founder President, TOGS

Dr. Saravana Kumar
Secretary, SOGS

Vote of Thanks

Dr. Vijayalakshmi Gnanasekaran
Treasurer, TNFOG

Co ordinator

Dr. Kalpana Balamurugan
Secretary, MOGS

TNFOG MARATHON CME

ON

Endometriosis

Date: 10th February 2023 (Friday) Time: 04:30 PM - 07:30 PM

Time	Topic	Faculty
04.30 PM - 05.00 PM	**Inauguration**	
	Introduction	Dr. S Sampath Kumari
	Tamilthai Vazhthu & Lamp Lighting	
	Welcome Address	Dr. Revathy Janakiram
	Address by the Chief Guest	Dr. Hrishikesh D Pai, President FOGSI
		Dr. Madhuri Patel, Secretary FOGSI
		Dr. Cynthia Alexander
	e Newsletter Release	
05.00 PM - 05.40 PM	**Session- 1 - YUVA SESSION**	
	Judges: Dr. Nidhi Sharma & Dr.Vijayalakshmi Kandasamy	
05.00 PM - 5.15 PM	Pathophysiology Endometriosis	Dr. Krithiga Meenakshi J
05.15 PM - 05.30 PM	Investigation of Endometriosis	Dr. Swathisree
05.30 PM - 05..40 PM	Q & A	
05.40 PM - 06.30 PM	**Session - 2: Scientific Session**	
	Chairpersons : Dr. Banumathy. M & Dr. Vani Pujari	
05.40 PM - 06.00PM	Medical Management of Endometriosis	Dr. Asha Rao
06.00 PM - 06.20 PM	Endometriosis and Infertility	Dr. Anu Chawala
06.20 PM - 06.30 PM	Q&A	
06.30 PM - 07.15 PM	**Session 3: Panel discussion on Adenomyosis**	
	Moderator	Dr. Ramani Devi T
	Panelists	Dr. Manonmani R Dr. Shanthi Rani B Dr. Sadhana Devi Dr. Nirmala Vijayakumar Dr. Rajapriya Ayyappan Dr. Grace M Dr. Radha Madhavi Dr. Saravana Kumar
07.15 PM - 07.20 PM	Vote of Thanks	Dr. Vijayalakshmi Gnanasekaran
	Co ordinator	Dr. Kalpana Balamurugan

After Each Session, Answer the 'Question' FIRST & GET EXCITING PRIZE!

For All Registrants, Certificate will be Provided

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PATHOPHYSIOLOGY OF ENDOMETRIOSIS

Dr. J. Krithika Meenakshi

MS, MRCOG, FMAS, DNB, MNAMS, FCR, CIMP, DRM

ICOG Certified Fertility Specialist

Consultant, Nanganallur Maternity & Fertility Center.

Introduction:

Endometriosis is a **common, benign, inflammatory** disease that includes the presence and growth of dysfunctional endometrial glands and stroma often with **reactive fibrosis and muscular metaplasia** outside the uterus, The etiopathogenesis of endometriosis is a multifactorial process that leads to the development of an extremely heterogeneous disease characterized by the variable acquisition and loss of cellular functions.

Theories:

It is considered as disease of theories. Classically, three theories exist to explain the etiology of endometriosis: 1) Sampson's theory, 2) Meyer's theory, and 3) Halban's theory. The most often quoted theory, and to date the one supported by the most evidence, is Sampson's theory of transplantation and implantation.

Stem Cells

Its origin would appear to be from **Müllerian or non-Müllerian stem cells with endometrial differentiation** that can potentially originate from **stem cells** of the endometrial basal layer, present in Müllerian remnants, in the blood originating from bone marrow, or from the peritoneum. These stem cells have the ability of the endometrium to regenerate cyclically by mechanisms of tissue regeneration and angiogenesis in response to hypoxia, which seem to play a key role when they are dysregulated in the development of endometriosis. What determines the presence of

such cells in the peritoneal cavity can occur during the **development of the embryos as well as during each menstrual cycle**, and what leads to the development of endometriosis is a complex process in which play a large number of interconnected factors potentially both **inherited and acquired**.

Genetic Infleunece

Genetic studies have confirmed that endometriosis has **a genetic nature,** but at the same time, this predisposition is complex. It is constituted by the combined action of several genes with limited influence. At the same time, the epigenetic mechanisms underlying endometriosis control many of the processes of acquisition and maintenance **of immunologic, immunohistochemical, histological and biological aberrations** that characterize both the eutopic and ectopic endometrium in patients affected by endometriosis.

However, what triggers such epigenetic alterations is not clear and may be both genetically and epigenetically inherited, or it may be acquired by the particular combination of several factors linked to the **persistent presence of menstrual reflux** in the peritoneal cavity as well as exogenous factors playing a critical role. Once started, the process is variable and can lead to the development of endometriosis through the progressive acquisition of alterations to the physiological processes of the endometrium, including the altered **hormonal physiology**, and modulating the interaction between endometriosis and the inflammatory response by subjugating it.

Conclusion

Research targets on identification of pathogenesis using a combination of unique and specific diagnostic biomarkers & genetic markers which can identify novel therapeutic targets that will pave a path for better early diagnosis and more effective treatment of endometriosis.

EVALUATION OF ENDOMETRIOSIS

Dr. Alagu Sakthi
SMMCH & RI

Diagnostic evaluation of endometriosis includes Physical examination, Laboratory testing, Diagnostic imaging, Diagnostic Laparoscopy, and pathologic analysis.

Physical Examination:

It may not reveal any abnormality in minimal lesions, but larger and advanced lesions can be detected by proper physical examination. On Abdominal examination- a mass may be felt which is tender. Per speculum may show blue or red powder burn lesion on cervix or posterior vaginal fornix. Bimanual examination-utero sacral ligaments nodularity and tenderness, uterus - retroverted, fixed, and tender or a Cystic adnexal mass which may be an endometrioma. Per rectum examination to look for Tender nodules in POD. Examination is mostly inaccurate in assessing the extent of endometriosis and if the lesions are extragenital.

Laboratory Finding:

These are not specific for endometriosis. To exclude infections or pregnancy complication an initial complete blood count, HCG, urine routine and culture vaginal and cervical swab is done.

CA-125 is an antigenic determinant and is elevated in endometriosis but it is not specific because it is elevated other pathology involving the fallopian tube epithelium, endometrium, endocervix and peritoneum. The levels are elevated and correlate with disease severity.it has poor sensitivity in detecting mild endometriosis but better diagnostic test for stage 3 or stage 4.

CA 125 levels in non-menstrual phase in women without endometriosis is 8 to 22 U/ml, In those women with mild to moderate endometriosis is 14-31 U/ml and in women with moderate to severe endometriosis is 13-95 U/ml.

Other biochemical markers-VEGF, CYTOKINES AND INTERLEUKINS (IL-6 & 8) but all these do not provide disease accuracy. Recently Micro RNA'S are used in diagnosing endometriosis. It is a non -invasive diagnostic tool. They are RNA oligonucleotides essential for modulating gene expression. several Micro RNA'S are differentially expressed in endometriosis such as MiR 125b-5p and let-7.

Diagnostic Imaging:

Trans vaginal ultrasound (TVS) is an initial imaging tool. It has accuracy for detecting endometriosis and to exclude other pelvic pathology. An endometrioma appears as a unilocular or a multilocular cyst with thin internal septations, homogenous low level internal echoes-ground glass appearance and a hyperechoic focus on cyst wall. Colour TVS doppler may show peri cystic flow.

CT scans are not routinely used as it will not pick up small peritoneal implants but can be used in abdominal wall endometriosis and thoracic endometriosis. MRI scan is used to for detecting peritoneal lesion of more than 1 cm, rectovaginal endometrial deposits and endometrioma.

Special conditions-Endorectal ultrasonography to find rectovaginal deep infiltrating endometriosis, BARIUM studies in case of bowel endometriosis and intravenous urography for ureteric or bladder endometriosis.

Diagnostic Laparoscopy:

Inspection of pelvis with laparoscopy is the gold standard for the diagnosis of endometriosis. It is a primary method used for diagnosing endometriosis. Laparoscopic findings include discrete endometriotic lesions, endometrioma or adhesions. Endometrial implants -blue, black powder burn deposits on pelvic organs and peritoneum. It can be used as both diagnostic and therapeutic.

<u>Role of laparoscopy in endometriosis:</u>

- Visualisations of lesions.
- Staging of the disease.
- Biopsy for histology.

- Evaluation of the extent of adhesions.
- Therapeutic intervention if required.

Patholgic Analysis:

Current guidelines do not require biopsy and histology for diagnosing endometriosis. Histology of endometriosis requires both endometrial glands and stroma outside uterine cavity. The gross appearance of endometriotic lesion often suggests microscopic findings, red lesions are vascularized and white lesions are fibrosed and have few vessels.

Cyclic and progressive pain without other clear etiology reflects endometriosis and clinical diagnosis with initiation of therapy is reasonable.

Tamil Nadu Federation of Obstetricians & Gynaecologists

ADOLESCENT ENDOMETRIOSIS

Dr. M. Gomathy

MBBS, MD (OG), DNB (OG)

"It's not just a bad period"

Endometriosis is the leading cause of secondary dysmenorrhea in adolescent. Endometriosis can occur as young as 8 years of age. Adolescent endometriosis is also the most common cause of chronic pelvic pain in adolescent. It should be considered in patient with persistent clinically significant dysmenorrhea despite treatment with hormonal agents and non-Steroidal anti-inflammatory drugs particularly if no other aetiology of chronic pelvic pain or secondary dysmenorrhea has been identified based on history, physical examination and pelvic ultrasonography.

Adolescent endometriosis is considered as inflammatory mediated estrogen dependent disease. Estrogen is produced by ovaries as well as Estrogen produced by endometrial implants due to aromatase activity promotes increased prostaglandin production resulting in pain.

Prevalence

The true prevalence of endometriosis is unknown, rough estimate to be 49 % to 75 % of adolescents.

Symptoms/ Clinical Presentation

The most common symptoms of the disease are acquired or progressive dysmenorrhea, acyclical and cyclical pain, heavy and irregular periods, dyspareunia in sexually active

girls, pain with bowel and bladder function and pain affecting quality of life. Symptoms associated with dysmenorrhea include nausea, vomiting, diarrhoea, headache, muscle cramps and poor sleep quality. Dysmenorrhea is the leading cause of recurrent short term school absenteeism for adolescent girls.

Pathophysiology

There are several theories regarding the pathogenesis, with Sampson's theory being the most widely accepted. According to Sampson's theory of retrograde menstruation, viable endometrial cells flow backwards through the fallopian tubes and seed inside the peritoneal cavity during menses. Various studies support this theory, including the implantation and growth potential of endometrial tissue in vitro the identification of endometrial implants in the posterior cul-de-sac, left hemipelvis, and right diaphragm also corresponds to gravity and the clockwise circulation of peritoneal fluid. However, up to 90 percent of healthy women demonstrate retrograde menstruation during laparoscopy, and most women do not develop endometriosis, suggesting other factors are likely involved. Several theories propose implants arise from tissues outside the uterus, such as stem cells or coelomic metaplasia. Spread of ectopic endometrial tissue has been hypothesized to occur through the lymphatics and vascular system. Genetic/epigenetic alterations from oxidative stress, hormonal signalling, and evasion from immune clearance have also been implicated. Lastly, neonatal uterine bleeding has been proposed to explain the endometriosis identified in pre-menarchal girls. The origin of endometriosis is likely multifactorial given the variable presentations.

Diagnosis

Adolescents are particularly susceptible in accessing medical care. Only 38% of those with adolescent endometriosis have symptoms before the age of 15 years, however it takes an astounding average over 9 years to receive correct diagnosis and treatment. Initial evaluation of an adolescent for endometriosis should begin with a comprehensive medical, gynaecological, menstrual, family and psychosocial history to determine whether the patient has primary dysmenorrhea, a pelvic examination is not necessary.

A pain diary is useful in documenting the frequency and character of pain, and if there are any provoking factors including menses or bladder/bowel function. Next, a physical exam

can be performed, with the goal to rule out a pelvic mass or a reproductive tract anomaly. A rectal abdominal exam may be better tolerated than a vaginal-abdominal exam, particularly if an adolescent if not sexually active. A pelvic exam is not always necessary; if there is concern for an obstructive anomaly, a q-tip can be inserted into the vagina to assess the vaginal length and patency.

Despite its prevalence, it is often misdiagnosed or considered as normal pelvic pain and the fact that endometriosis rarely shows up on a diagnostic test. That is the patient must undergo a laparoscopic surgical evaluation in-order to diagnose endometriosis, the parents and gynaecologist hesitate to put for invasive laparoscopy for diagnosis. Gold standard in diagnosis of adolescent endometriosis is histological examination of specimen collected from the suspicious areas (endometriotic spot) during laparoscopy.

The laparoscopic appearance of endometriosis may differ in an adolescent than in adult. In adolescent the endometriosis lesions are typically clear or red or white and/ or yellow brown lesions more frequently than black or blue lesion ("Powder burn") lesion in adult women which can be difficult to identify for the gynaecologist unfamiliar with endometriosis in adolescent. Subtle clear lesions of endometriosis may be better visualised by filling the pelvic with irrigation fluid.

Ultrasound is helpful in diagnosing ovarian endometriosis, but not useful for non-ovarian endometriotic lesion. Endometriosis requires either a surgical and pathological diagnosis in adolescents, hence suspected adolescent with persistent dysmenorrhea despite treatment or no other identified aetiologies should be counselled about the high likelihood of endometriosis and risks and benefits of diagnostic laparoscopy. The benefits of laparoscopy is confirmation of diagnosis and to rule out other causes of chronic pelvic pain.

Laparoscopy not only gives opportunity to diagnose but also give opportunity to treat endometriosis with coagulation, ablation and resection of visible implants and histo-pathological examination. In adhesive endometriosis disease, adhesion are treated by lysis of adhesion.

Treatment

Endometriosis in adolescent is a chronic disease with potentially progressive, if left untreated. The goals of the therapy include.

- Symptom relief
- Suppression of disease progression,
- Protection of future fertility.

Endometriotic therapy must be individualized. In adolescent, endometriosis requires may long term medical treatment till the time they complete the childbearing. Psychological support is very essential. The first line of treatment for surely diagnosed and treated laparoscopic endometriotic lesion or presumed endometriosis requires hormonal suppression therapy using progesterone only protocols, levonorgestrol or combined contraceptive pills which ever type they best fit. They should be on continued hormonal suppression unless trying for pregnancy. Still if the pain is unresponsive adolescent may benefit from GnRh agonist therapy and add-back treatment for 6 months. Adolescent endometriosis patient may often benefit from ongoing education programme, supportive treatment with integration of multi-disciplinary approach like biofeedback, pain management, acupuncture and herbal treatment.

Early diagnosis and treatment may protect the adolescent's future fertility. All healthcare providers must be aware of the existence of adolescent endometriosis. Long term medical therapy will hopefully decrease pain and progression of the disease.

Tamil Nadu Federation of Obstetricians & Gynaecologists

Endometriosis and Sexuality

Dr. Jeyarani Kamaraj

President, OGSSI

Introduction

Endometriosis is a global disease affecting 5–15% of women during their reproductive years and endometriosis is also a disease that affects young, sexually active women during different phases of their sexual life and during development of their sexual behaviour. Consequently, sexual health is a major concern for endometriosis patients and should also be a primary concern in endometriosis care and research and as it is a chronic, prolonged, recurrent disease that affects young women, it is absolutely necessary to bridge the artificial divide between reproductive and sexual health in endometriosis patients and their partners.

Sex is the very important foundation of existence. Sexual functions are vital and mandatory in infertility management. Human sexuality is a complex phenomenon driven by social, psycho-logical and biological/hormonal factors. Sexual health is a critical aspect of quality of life and is also influenced by medical conditions and health-care interventions, particularly in women with gynaecological disorders like endometriosis and gynaecological cancers, as they involve the organs of sexual functioning and organs integral to sexuality and femininity.

Sexual Health

Sexual Health is a state of physical, emotional, mental and social well-being related to sexuality. It is not merely the absence of disease, dysfunction or infirmity.

Sexuality

Is experienced and expressed in thoughts, fantasies, desires, beliefs, attitudes, values, behaviours, practices, roles and relationships.

Sexual Response

Sexual response has the requisite biological underpinning, but it is usually experienced in an intrapersonal, interpersonal and cultural context. Thus, Sexual function involves a complex interaction and biological, sociocultural and psychological factors. It is a sequence of physiological events, including sexual desire, arousal and genital responses.

Prevalence of female sexual dysfunction in endometriosis

Prevalence of female sexual dysfunction was 73%. Potential predictors for female sexual dysfunction: Pelvic pain intensity OR 3.4. Die OR 4.1 Stage III-IV OR 4.4

Sexual Dysfunction & Endometriosis

Chronic pelvic pain is the main symptom leads to inactivity and might also result in severe damage to body image, sexuality, higher levels of anxiety and depression and poor quality of life. The Study conducted by De Sepulcri et al study demonstrated endometriosis patients, 86% showed depressive and 87% showed anxiety symptoms. Over a long period of time the painful sexual function may further result in a lack of desire, arousal difficulties etc.

International cross-sectional survey by De Graaff et al demonstrated that 47% of endometriosis patients experienced dyspareunia and had negative effect on the mental and physical health domains in the SF36 questionnaire. Endometriosis itself and the delay in diagnosis and management are associated with reduced health-related quality of life (QoL) and productivity. Endometriosis appears to impact all domains of sexual function, desire/arousal, orgasm, satisfaction, and pain, leading to sexual dysfunction and distress in 70–75% of patients, at least in advanced/chronic cases- evidence by limited studies.

Cumulative prevalence of sexual dysfunction using the FSFI and FSDS were 32% and 78%, respectively, with a significant correlation between stage of disease, dyspareunia and score on both questionnaires (56% of patients had sexual dysfunction at AFS stage

4). When sexual dysfunction was diagnosed, patients also had a significantly fewer episodes of sexual intercourse per month and greater fear of separation because of coital pain than patients without sexual dysfunction. Compared with the patients with no to mild pelvic pain, those with moderate-to severe pelvic pain had a 3.4-fold (CI 1.3–8.8) higher risk of sexual dysfunction. Patients with stage III or IV had a 4.4-fold (CI 1.3–15.5) higher risk than those with stage I or II. Advanced states of endometriosis affects the desire domain, in addition to sexual satisfaction, orgasm and pain.

Important biological and psychosocial variables

Dyspareunia can be considered the first step in the development of sexual dysfunction; additional factors characterize the evolution towards an impairment of sexual health. According to the fear-avoidance model, multiple biopsychosocial variables influence sexual distress.

Sexual Pain induce FEAR-AVOIDANCE model

Sexual pain in endometriosis patients induces a fear-avoidance reaction, leading to arousal/desire disorder and sexual distress in the majority of patients. Biopsychosocial variables of sexual pain play a critical role in the fear-avoidance model.

Management of endometriosis

Management of endometriosis often unexplored as the clinicians are reluctant to address the issue, because deficits in communication skills, unrealistic fear of offending the patient, discomfort to a patient of opposite gender, time constraints in busy clinic practice, inadequate training and knowledge gap.

Management of dysfunction related to endometriosis should take into account its important psychological and interpersonal effects. A multidisciplinary view is advisable while designing individual treatment plans for this large group of affected women and their partners. It would require an integrated approach, combining

1. Medical,
2. Counselling,
3. Psychological interventions,

4. Lifestyle changes and

5. Psychotherapy.

Definitely the psychosexual issues in endometriosis have to be recognized and the severity has to be assessed before planning the management. This includes

1. Detail Medical History – to rule other causes causing FSD like depression, diabetes, drug and etc.

2. Sexual History – Detail sexual history about frequency, when problem started, its nature, in relation with menstrual cycle days and severity.

3. Psychosocial History – Life stress, Infertility stress and pain aggravating factors

4. Self Report Measures – to access the severity of sexual function.

ART IN ENDOMETRIOSIS

Dr. B. Kalpana

MBBS., MD (OG)

FNB (Reproductive Medicine)

MSc (Embryology)., Ph.D., FICOG, FIAOG, FICS

Incidence:

- General population 3-6%
- Among infertility – 20-50%
- Chronic pelvic pain – 15%
- Hysterectomy – 25%
- Sterilization – 6%

Advances In Imaging Technology:

- TVUS : 91% sensitivity and 98% specificity
- TRUS : Extent of involvement of wall of the bowel and distance from theanus
- MRI is also superior to ultrasound in diagnosing rectosigmoid lesions and endometriosis of the bladder.
- ESHRE guideline for the diagnosis and treatment of endometriosis.

Fecundity Rate:

- Fecundity rate in normal couple 20%
- Endometriosis 1-3% depends upon age and stage of disease

MAR:

Medically assisted Reproduction is defined as Reproduction brought about through ovulation Induction Controlled ovarian stimulation ovulation triggering ART, IUI, Intra cervical, Intra Vaginal insemination.

Endometriosis:

- COH ,IUI has been used in the treatment of couples with minimal and mild Endometriosis. Moderate, Severe endometriosis will need ART.

COH & IUI Vs IUI:

- RCT compared Gn+IUI with Urine LH timed IUI alone. 57 couples with minimal or mild endometriosis the PR was 5 times higher than IUI alone.

IUI:

- COH with Gn and IUI was assessed in a RCT including 103 Couples with minimal to mild endometriosis. 53 under treatment, 50 in the expectantgp. LBR was 5-6 times higher in the treated group.

Is IVF/ICSI Indicated in Endometriosis?

- Associated tubal factor
- Male infertility
- Failed IUI in minimal to mild endometriosis
- Failed IUI in Moderate to severe endometriosis of <35 years
- Moderate to severe endometriosis of beyond 35 years

COH & Oocyte Retrieval

- Decreased oocyte yield due to poor folliculogenesis. Decreased ovarianreserve in post-surgical cases. Technical difficulty

Protocol:

- RCT compared LP, ULP in 80 women.
- All Stages of endometriosis were included.
- No difference in PR between Protocols in minimal and mild endometriosis
- In Stage III, IV endometriosis PR higher in ULP (50%) Compared to LP (19%).

GNRH Analogues and ART:

- 3-6 cycles of GnRH analogues before IVF improves the outcome of pregnancy and reduces miscarriage
- GnRH modulates NK cells of uterus.

- Normalizes the endometrial aromatase expression OR 4.28 95% CI 2.00-9.15 3RCTs of 165 patients by

ANTAG Protocol:

- RCT incuding 246 women with minimal to mild endometriosis and endometrioma Showed that IR, PR with GnRH antag were not inferiorto GnRH agonist.

Is ICSI Better than IVF in Endometriosis:

Barnhat et al 2022 Reported less fertilization in IVF. Improved Stimulation and O.R techniques will increase oocyte yield which compensates reduced fertilization rate ICSI is always better than IVF.

ART in Endometriosis:

- In Natural cycle IVF
- Were similar in endometriosis and tubal factor.
- But higher than patients with
- Unexplained Infertility

Endometriosis:

- Systematic review compared PR in endometriosis, tubal factor. Review included 22 studies 2377 cycles with endometriosis 4383 with out endometriosis. Confounding variables adjusted.PR in Stage I, II were notsignificantly different from tubal factor.PR in Stage III, IV were significantly lower than for tubal factor. This is the only systematic review. Study period was Jan 1980 to May 1999.Different drugs were used. Technical Conditions were different. No correction was made for medical or Surgical treatment. Endometriosis does not adversely affect PR in large data bases (Society for Assisted Reproductive Technology SART) and Human Fertilization and Embryology Authority (HFEA).

DIE:

- 2 Studies of possible implications of deep endometriosis on the efficacyof IVF /ICSI showed conflicting results.

Risk of Ovarian Stimulation in Endometriosis:

- 4 Studies evaluated RR in
- Gn ovarian stimulation was not associated with increased risk of recurrence.

Adjuvant Medical Therapy with ART:

- Medical treatment of endometriosis prior to MAR may result in improved outcome, either because of improving Oocyte quality or endometrial receptivity. Cochrane review 2006 which included 3 Studies involving 228 patients concluded ULP increases the odd ratio of PR by four fold. LBR is also increased but the magnitude is unreliable. This review did not consider miscarriage rate, multiple PR, ectopic PR. Authors concluded that the quality of study was poor, there could be methodological bias, there is a need for high quality studies.

Adjuvant Surgical Therapy with ART:

- In peritoneal endometriosis, a retrospective cohort study reported that surgery might be useful to enhance the success of ART. 399 women withminimal to mild endometriosis all visible endometriosis was completely removed prior to ART. Control group (262 women) had only diagnostic laparoscopy. In Surgery group, IP, PR, LBR were significantly higher.

Endometriosis:

- However this does not imply that a laparoscopy should be performed prior to ART in all asymptomatic women with the only aim to diagnose and subsequently treat peritoneal endometriosis to improve ART outcome. Stage I, II endometriosis undergoing laparoscopy prior to treatment with ART, Clinician may consider the complete Surgical removal of endometriosis to improve LBR, although the benefit is not well established.

Surgery For Ovarian Endometrioma Prior to ART:

- Cochrane review of 4 RCT involving 312 women concluded that laparoscopic aspiration or cystectomy of endometrioma prior to ARTdoes not show any benefit with regard the PR.

Endometriosis:

- Based on no difference in PR, some authors advise cystecomy, whereas others advise caution with surgery because of the harmful effect on Ovarian reserve. In endometrioma larger than 3cm, GDG recommends to consider cystectomy prior to ART to improve endometriosis associated pain or the accessibility of the follicle. The decision to proceed with surgery should be considered carefully if the women has had previous ovarian Surgery.

Is There A Role of Surgical Treatment of Endometrioma Prior To IVF?

Laparoscopic ovarian cystectomy is recommended for endometriomas > 4 cm. Important to balance the benefits Vs potential damage to ovarian reserve, apart from risk associated with surgery. Post-surgical patients need more gonodotrophins and reduced E2 levels. But no difference in implantation rate PR and miscarriage.

Evidence Not In Favour of Endometrioma Excision:

Garcia – Velasco et al 2004 in a retrospective study compared the outcome inpatient with ovarian cystectomy for cyst> 3 cm Vs No treatment.

Patient who had surgery required more gonadotrophins and had decreased E2. No difference as regards the implantation rate, Pregnancy and miscarriage.

Current Recommendations – Not In Favour of Excision:

Asymptomatic endometrioma < 4cm IVF is Preferred

Advantages:

- Shorter time
- Reduced cost
- Reduced surgical risk
- Treats multiple problems
- Ideal in elderly women

In Favour of Endometrioma Excision:

- Symptomatic women should undergo excision can be counselled that with surgery her chances of successful IVF outcome will not decrease. Risk of surgery is minor. Recurrence rate is 20-30%. Less than 3% chancesof premature ovarian failure. With large endometrioma O.R may be difficult with possibility of infection and follicular fluid contamination. Possibility of occult malignancy to be kept in mind.

Surgery Prior To ART In DIE:

- Surgical therapy for DIE is mainly performed because of pain. Effectiveness of surgical excision of deep nodular lesion before ART isnot well established with regard to reproductive out come.

LAP Surgery:

- PR after repeat surgery lowest, half that after first surgery and 2 cyclesof IVF might be more effective.

Surgery Vs IVF For Recurrent Moderate To Severe Endometriosis:

Recurrent Endometriosis is addressed by ASRM which suggests IVF Instead of second line Surgery.

Oocyte Cryopreservation:

- COH & Oocyte retrieval for egg banking and fertility preservation could be a good option for those young women who needs extensive surgery. Counsel about risk of surgery Vs limitation of egg banking. Vitrification is ideal. Oocyte cryopreservation in case of nulliparous young woman with severe endometriosis has been successfully performed.

Preserving Fertility In Endometriosis:

- In young women undertaking surgery consider discussing:
- Measuring AMH and planning pregnancy
- Cryopreserving oocytes
- Freezing ovarian tissue at excision of endometrioma
- At this stage little research re outcomes

Results of Meta Analysis of IVF In Endometriosis:

22 Studies –2377 IVF cycles for endometriosis –4383 without endometriosis. Lower Pregnancy rate OR 0.56; 95% CI(0.44 -0.70). Lower PR in severe disease Vs mild disease OR 0.6; 95% CI (0.42 – 0.87)

Conclusion:

- Endometriosis compromises fertility by several mechanism
- ART overcomes and achieves pregnancy except poor oocyte and embryoquality
- Endometrial receptivity not altered.
- Surgery decreases ovarian reserve, hence weigh potential benefit overreduction in OR

- Surgery is indicated in symptomatic women.
- Careful surgery does not compromise ovarian reserve.
- Results of ART are comparable to tubal factor and unexplained group.
- COH with IUI improves pregnancy rate compared to expectant management.
- IVF is more effective than repeat surgery (or) expectant management.
- Work with donor oocytes suggests that quality of oocyte is a greaterproblem than implantation.

Tamil Nadu Federation of Obstetricians & Gynaecologists

MEDICAL MANAGEMENT OF ENDOMETRIOSIS: IN NEED FOR CURATIVE RATHER THAN SUPPRESSIVE THERAPY

Dr. Asha R. Rao

Dr. Rajeshwari

Endometriosis is an estrogen dependent chronic, debilitating, recurrent disease with painful symptoms such as chronic pelvic pain, dysmenorrhoea, dyspareunia, dysuria, dyschezia, infertility, fatigue which is having negative impact on the overall quality of women's life. Studies also suggests these women have higher rates of depression, anxiety, emotional distress. It affects 1 in 10 women of reproductive age.

Endometriosis can be suspected without surgical exploration. Diagnosis of endometriosis should no longer be considered as synonym of immediate surgery and initiation of empiric treatment with early recognition of the disease prevents long-term morbidity such as chronic pain and preserve fertility. Medical therapy can be initiated without histological confirmation.

The medical management of endometriosis is targeted towards controlling pain and suppression of hormonally active endometriotic tissue. Over years, several therapeutic options have been developed and successfully used to achieve these aims and newer targets are being developed at a fast pace.

Indications of medical management include relief of pain, prevention of long term and post-surgical recurrence of disease if not planning for pregnancy and before ART if required. There is no role for medical therapy in women desiring fertility and pre-operatively.

A trial of non- steroidal anti-inflammatory drugs (NSAIDs) initially can be helpful in controlling the pain associated with dysmenorrhea. Hormonal therapies that rely on suppression of the endometriotic tissue include combines oral contraceptives, progesterone only contraceptives, GNRH agonists, aromatse inhibitors and danazol.

Although quite successful, they have unwanted side effects secondary to hormonal suppression and need to be closely monitored.

All the currently available medications give a temporary relief of symptoms rather than cure, as on treatment discontinuation recurrence is the rule and also they are contraceptive in nature as they mediate its action via blocking HPO axis, thereby suppressing ovulation and estrogen production. And hence it's a challenge for endometriosis patients with painful symptoms to get pregnant.

The treatment selection depends on therapeutic effectiveness, tolerability, drug cost, the physician's experience and expected patient's compliance.

Oral Contraceptive pills

The first line treatment in those who do not wish to conceive in near future is combined hormonal contraceptives (COC) which can be used in continuous fashion for better pain relief with analgesics as needed. Available as pills, transdermal patches, vaginal rings.

A review by Grande et al., (2019) concluded that COC results in a statistically significant reduction in endometriosis related pain resulting in improvement in quality of life.

Progestins

Progestin-only therapies are another first line option. Dienogest, norethidrone acetate, medroxyprogesterone acetate has comparable efficacy with GnRH agonists and lesser side effect than that. The LNG-IUS or ETONOGESTREL subdermal implants helps in reducing pain and achieve **long term medical management.**

Dienogest is now increasingly preferred for long term management of endometriosis, its effectiveness in pain relief is comparable to GnRH agonists but with less side effects on bone loss. Dienogest is prescribed at 2 mg once daily dosage with no break. It can be

started at any day of the cycle. It can be used safely upto 1 year in adolescents. The long-term safety of Dienogest upto 3-7 years is being studied by the Vipos study.

A systematic review of RCT by Lan et al., (2013) comparing LNG IUS with GNRH agonist found that LNG IUS has reduced pain scores with no difference compared with GNRH agonist.

GnRH agonists

ESHRE recommends GnRh agonist with add back therapy as second line of management to reduce endometriosis associated pain who do not respond to first line regimen although evidence is less regarding duration and dose of treatment. They are prescribed as second line due to their serious side effects on bone and cost. However, women who are desirous of pregnancy with chronic pain, where ivf is required, GNRH agonist with add back therapy is the appropriate choice.

Aromatase Inhibitors

In women with endometriosis associated pain, refractory to other medical or surgical treatment, ESHRE recommends to prescribe aromatase inhibitors . It can be prescribed in combination with OCP, GnRH agonist / antagonist. Letrozole with progestin add back lead upto 75% reduction in endometrioma volume and improved pain symptoms after 3 months of treatment (Agarwal et al., 2015).

Danazol

Danazol is no longer recommended for pain relief in endometriosis due to its side effects. Transvaginal danazol preparation is under study for its usefulness in DIE and the side effect profile is under evaluation.

Newer drugs

Emerging medical treatments are GNRH antagonist, SERM, SPRM, immunomodulators , anti-angiogenic drugs.

GnRH Antagonist (Elagolix / cetrorelix) has acceptable safety and efficacy in phase 2 RCTs.

Selective Progestrone receptor modulators (SPRM) such as Mifepristone , asoprisnil , UPA , Tanaproget has shown significant reduction in dysmenorrhea ,although long term efficacy needs further studies.

Selective estrogen receptor modulator (SERM) such as raloxifene, bazedoxifene has shown significant reduction of endometriotic implants in animal studies ,effectiveness in humans yet to be evaluated.

Non-hormonal immunomodulators such as etanercept, infliximab, IFN-2b, lipoxin, rapamycin, loxoribine are acting against inflammatory mediators like TNF-alpha, NK CELLS, VEGF are now under study in non-humans.

Similarly, antiangiogenic drugs against VEGF like statins, cabergolin, bromocriptine, quinagolide, glitazones are under trial. A study in 2014 (amr et al) showed cabergoline yields better results in decreasing the size of endometrioma compared to LHRH agonist.

Ideally, medications for endometriosis should be curative rather than suppressive. They should effectively treat pain, with acceptable side effects, long term use should be safe and affordable. Moreover, they should not be contraceptive, not to interfere with ovulation and normal implantation in spontaneous conception with no teratogenic potential. They should suppress the growth of already existing lesions and prevent the development of new ones to limit the need for repeat surgery and complications associated with advanced endometriosis.

More research into local neurogenesis, central sensitisation and the genetics of endometriosis may provide future targets. Endometriosis has a highly variable phenotype and thus a wide variety of medical treatments targeting different pathways is likely to be important to move toward precision health (personalised medicine) in endometriosis.

ADENOMYOSIS AND IMPACT ON FERTILITY

Dr. T. Ramani Devi

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Vice President FOGSI 2020

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Adenomyosis is the presence of ectopic endometrial glands and stroma within the myometrium.[1] This glandular tissue cause dysmenorrhea due to repeated collection of blood and leads to hypertrophy and hyperplasia of the surrounding myometrium, causing uterine enlargement. This also leads to AUB.

Incidence of Adenomyosis

Adenomyosis is diagnosed in 22% of infertile women less than 40 years undergoing ART. Adenomyosis is no longer considered to occur in women over 40 years of age, but it also affects 30% of young women. Incidence is increased due to non-invasive diagnostic modalities like USG and MRI. It is seen in association with endometriosis (21.8%-70%), fibroids (50%), endometrial hyperplasia (35%), endometrial carcinoma (2%) and sub fertility (28%).

Pathogenesis

Downward invagination of the endometrial basalis layer into the myometrium is the common etiology. Leyendecker et al 2011 showed that uterine auto-traumatization and the initiation of the mechanism of tissue injury and repair (TIAR) as the primary cause for adenomyosis.[2]

Clinical presentation

Women present with heavy menstrual bleeding, intermenstrual spotting, dysmenorrhea, dyspareunia and sub-fertility, due to altered uterine peristaltic activity, endometrial receptivity and impaired implantation.

Types of adenomyosis

Types of adenomyosis are diffuse adenomyosis and focal adenomyoma. Diffuse adenomyosis is common in multiparous women and focal adenomyoma is seen in nulliparous women. Adenomyosis is graded into superficial, intermediate and deep as per myometrial involvement.

Clinical examination

Bimanual pelvic examination shows uniform enlargement of the uterus or irregularity if there is associated fibroids. Pelvic tenderness is also associated with diffuse enlargement of uterus.

Diagnosis of Adenomyosis

It is mainly by USG and in doubtful cases by MRI. It will be a globular or bulky uterus with indistinct endo-myometrial junction. The junctional zone is indistinct and greater than 12 mm in thickness. Speckled appearance, myometrial linear striations are seen. Doppler ultrasound shows increased flow and penetrating vascularity.[3]

MRI features suggestive of adenomyosis include junctional zone (JZ) thickness of more than 12mm, high signal foci within areas of low signal intensity, linear striations of increased intensity radiating from endometrium into myometrium are seen. Hysteroscopy, HSG, CA 125 and HPE can aid in diagnosis.[3]

Adenomyosis and infertility

The presence of adenomyosis in young women and associated endometriosis are proven to be the cause for subfertility. There is increase in P 450 aromatase, estrogens and PGE2 which may lead to uterine hyper-peristalsis, alteration of tubal sperm transportation, alteration of embryonic implantation, endometrial function and receptivity, gene

dysregulation of endometrial proteins, abnormal concentrations and increased production of intrauterine ROS. Increased ROS explains the increase risk of preterm delivery in patients with adenomyosis.[4] Patients have greater stromal macrophages density which increases TNF alpha, IL 1, IL 6, miRNA, IL 10 and increased ROS. There is over expression of ERα receptor and down regulation of progesterone receptor A & B which results in progesterone resistance. Over expression of ERα reduces β-v3 integrin secretion which alters uterine receptivity.[5]

Management of subfertility

This includes medical, surgical management and ART.

There can be spontaneous conception in women with focal adenomyosis.

Role of GnRH analogues

They are effective in reducing the size of the lesion and facilitate fertility. Spontaneous pregnancy can occur after GnRh analogues.[6]

Adenomyosis and ART

Since adenomyosis is seen in late 30 & early 40, these patients are suitable for ART. Two staged ART is suitable. Ovulation induction with antagonist protocol followed by FET in subsequent cycle is the modality of treatment.[7] Prior to FET, GnRH analogue for 3-6 cycles, optimizes ART outcome. GnRH analogue decreases expression of aromatase, cytochrome P450 in the eutopic endometrium of women with adenomyosis and endometriosis. It is also known to decrease the expression of nitric oxide synthases.[8]

Aromatase inhibitors

Combined use of aromatase inhibitors with GnRH analogues, reduction in uterine volume of 60% was observed after 8 weeks of treatment. This has to be combined with progesterone to reduce vasomotor changes. Dienogest can be added to GnRH analogues and letrozole instead of norethisterone. As the duration of treatment is only for a period of 3 months, there may not be much reduction in BMD, but addition of calcium and Vitamin D3 might help.

Mirena

LNG-IUS may be used in conjunction with other treatment modalities such as GnRH analogue for a short period in patients with endometrial hyperplasia.

Non-surgical management of adenomyosis

Uterine artery embolization and MRI-assisted high-intensity focused ultrasound (HIFU) ablation are not suitable treatment in infertility.

Role of uterine-sparing surgery in adenomyosis

It is suitable for patients with AUB (Not responding to medication), severe dysmenorrhoea, recurrent abortion and ART failures due to implantation failure. This can be focal excision of adenomyoma or volume reduction surgery like Osada's procedure.[9] Laparotomy or Laparoscopy can be done. There is always a risk of rupture of uterus during pregnancy and hence, pregnancy should be planned after 6 months. Japanese study the clinical pregnancy rate was 41.3% in those aged < 39 years and 3.7% in those aged > 40 in patients treated with conservative surgery.[10]

IVF protocols for adenomyosis

Both agonist and antagonist protocols have the same outcome regarding clinical pregnancy rate, miscarriage rate and live birth rate. GnRh analogue pretreatment is more potent in FET, in a lower estrogenic state, than in the fresh ET cycles.[11]

Precautions to be followed prior to embryo transfer

Uterine volume has to be reduced and the thickness of the JZ should be less than 8 mm which is possible by GnRH analogues pretreatment. Pre transfer assessment by hysteroscopy and mock transfer helps in easy transfer. In patients with increased myometrial contractions, oxytocin antagonist like Atosiban can be tried. It is also preferrable to do single embryo transfer.

Adenomyosis and IVF outcomes

Uterine adenomyosis has lower implantation rate, clinical pregnancy rate and birth rate, higher abortion rate in patients undergoing IVF – ET. Implantation rate is not impaired in asymptomatic women who are diagnosed with adenomyosis at TVS.

ART with donor egg program

Adenomyosis when co-exists with endometriosis, elderly women > 35 years or in previous endometriosis surgery with poor ovarian reserve might need donor egg program. In this situation also, JZ thickness has to be reduced to <8 mm. Precautions as mentioned previously has to be followed. Still the results are guarded.

Conclusion

Adenomyosis is a challenging condition to treat in the scenario of subfertility. It is interesting to note that with ART and use of GnRH analogues pre-treatment, two staged ART, there are better pregnancy rate and reproductive outcome in adenomyosis. Surgical treatment has selective role as the incidence of rupture uterus is high.

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TNFOG

Past Events

TNFOG - BODHANA
PG Case Discussion

On 28th January 2023, Time: 5.30pm – 7.00pm

Topic: Fibroid

Welcome Address

Dr.Revathy Janakiram
President TNFOG

Case presenters

Dr .Srushti Ramesh
Final Year ,MS (OBG)

Dr. Dharani.S
Final Year ,MS (OBG)

Coordinators

Dr. Sampath Kumari.S
Secretary TNFOG

Dr. Kalpana.B
Secretary MOGS

Internal

Dr.M.Anuradha
Prof & HOD
SRM Medical College Hospital &
Research Centre

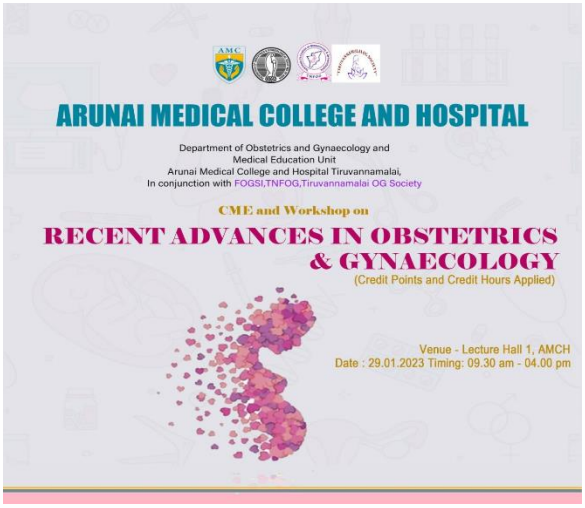
Dr Karthiga Prabhu J
Professor
SRM Medical College Hospital &
Research Centre

External

Dr. K.S.Chitra
Prof & HOD
Velammal Medical College Hospital &
Research Institute – Madurai.

Dr S Padma
Sr Consultant & HOD OF O&G
Meenakshi Mission Hospital &
Research Center – Madurai.

29th Jan 2023



The new office bearers of

Nagercoil Obstretic and Gynaec society

under the Aegis of TNFOG

conducted their installation meeting with the TNFOG president

Dr Revathy Janakiram and Dr Sunitha Tandulwadkar.

The meeting was attended by 95 members and both the speakers showcased academic excellence.

Tamil Nadu Federation of Obstetricians & Gynaecologists

Tamil Nadu Federation of Obstetricians & Gynaecologists

எளிய பரிசோதனை
இன்னுயிர் காக்கும்.

உங்களது ஆரோக்கியம்
எங்களது இலக்கு

மகளிர் நலம் மானுட பலம்

தமிழ்நாடு மகப்பேறு மற்றும் மகளிர் நோய் மருத்துவச் சங்கம்
மதுரை மகப்பேறு மற்றும் மகளிர் நோய் மருத்துவச் சங்கம்
திண்டுக்கல் மகப்பேறு மற்றும் மகளிர் நோய் மருத்துவச் சங்கம்
இணைந்து நடத்தும்

30 வயதிற்கு மேற்பட்ட மகளிருக்கான சிறப்பு இலவச மருத்துவ முகாம் அழைப்பிதழ்

தேதி : 04-02-2023 சனிக்கிழமை
நேரம் : காலை 9.00 மணி முதல் மாலை 5.00 மணி வரை
இடம் : வேடசந்தூர் அரசு ஆண்கள் மேல்நிலைப்பள்ளி

நிகழ்ச்சி நிரல்

தமிழ்த்தாய் வாழ்த்து

குத்துவிளக்கு ஏற்றுதல்

தலைமை :

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முகாமைத் துவக்கி வைத்து சிறப்புரை :

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நாட்டுப்பண்

Tamil Nadu Federation of Obstetricians & Gynaecologists

TNFOG

Upcoming Events

12th February 2023

Erode Annual conference (Magalir Nalam CME)

18th February 2023

Tirunelveli Annual Conference

25th February 2023

Previous LSCS (Bodhana) by Nagerkovil Medical College

Shield CONNECT