TURKISH ENDOMETRIOSIS & ADENOMYOSIS SOCIETY 2009

12th year 2009-2020

# ENDOMETRIOSIS BULLETIN

JUNE 2021 / ISSUE XVIII

**WE WOULD LIKE TO EXPRESS OUR GRATITUDE TO ALL OUR HEALTHCARE PROFESSIONALS WORKING ON THE FRONT LINES**

**1 in 10 Women are Affected by Endometriosis**

**www.endometriozis.org**

**PREFACE**

Hello,

We are with you again with our 18th issue.

While the Covid-19 pandemic continues all over the world, albeit at a decreasing rate, our activities for both patients and physicians continue during this period. You can find details about these activities in this month's issue of our newsletter.

In this issue, we included the abstracts of a French longitudinal study on the relation between endometriosis and assisted reproductive techniques and mother-child morbidities, of a review onnew herbal medicationsin the treatment of endometriosis, of a study on what immune-related factors can cause endometriosis, of the course of intestinal cancer in endometriosis, of a study on the relationship between endometriosisdepressionand stomach disorders, and the medical treatment of endometriosis. You will also be able to read the abstractof an up-to-date review onElagolix, which is thought to be a new medical treatment option for endometriosis.

In April, our 8th webinar titled as **'Endometriosis and Poor Perinatal Outcome Current Situation'** took place, which was chaired by **Levent Senturk** and **Ibrahim Bildirici**, where **Recai Pabuccu** and **Baris Mulayim** participated as speakersand shared their experiences with us. Our 9th live webinar, moderated by **Timur Gurgan** and **Yaprak Ustun** was about **'2021 update on the diagnosis of endometriosis'**, with the scientific contributions of **Sebastian Schafer** from Germany, **Gaby Moawad** from USA and **Pinar Yalcin Bahat** from Turkey.

The 22nd, 23rd, 24th, 25th, 26th, 27th and 28th Instagram question and answer series, which we started during the pandemic, continued with the participation of valuable experts **TanerUsta, Cem Atabekoglu, Umit Inceboz, Omer Lutfi Tapsiz, Murat Ulukus, Gazi Yildirim, Husnu Gorgen** and young group members of our association, **Karolin Ohanoglu, Aysegul Mut, Isik Sozen, Sebnem Alanya Tosun,Humeyra Demirkiran, Yusuf Aytac Tohma** and **ElifGoknurTopcu.**

At the 9th National Gynecological Endoscopy Congress and 3rd Young Endoscopists Symposium held between 1-5 June 2021, Taner Usta and Ahmet Kale organized a pre-congress event ‘Pelvic Pain Course’, which was carried out successfully with the participation of the members of our board of directors and specialist from different fields dealing with chronic pelvic pain.

During this period, the webinar series organized by the European Endometriosis League continued with the valuable presentations of **Mario Malzoni, Mohamed Bedaiwy** and **Mohamed Mabrouk** in April, May and June. The webinar series will continue with monthly presentations until the end of the year. You can reach the monthly webinar program from our newsletter.

In our next issue, we hope to share with you good news from all over the world and our country.

Best regards,

Board Members of Turkish Endometriosis & Adenomyosis Society

# Turkish Endometriosis & Adenomyosis Society Board of Directors 2019-2022

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**Endometriosis e-bulletin is prepared by Turkish Endometriosis & Adenomyosis Society. If there are any topics that you would like us to include in the bulletin or any questions you would like to ask, you can contact us via e-mail at drcihankaya@gmail.com.**

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# TABLE OF CONTENTS

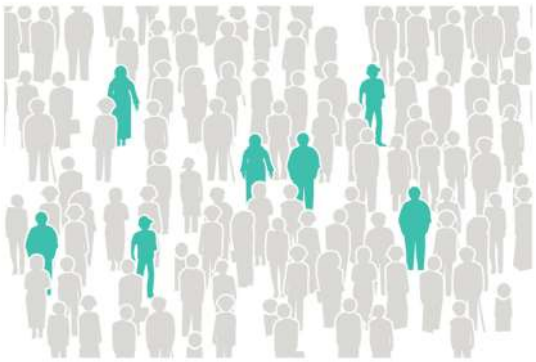
# A SELECTED ARTICLES

## 1 The epidemiology of endometriosis is poorly known as the pathophysiology and diagnosis are unclear

Philippe R Koninckx , Anastasia Ussia , Leila Adamyan , MunaTahlak , JörgKeckstein , Arnaud Wattiez , Dan C Martin

**Abstract**

As the diagnosis requires a laparoscopy, we only have data in women with pain and/or infertility. Endometriosis has been considered to be a single disease defined as 'endometrium like glands and stroma outside the uterus'. However, subtle, typical, cystic ovarian and deep endometriosis lesions should be considered to be different pathologies which occur in all combinations and with different severities. All large datasets, especially those based on hospital discharge records, consider endometriosis to be a single disease without taking into account severity. In particular, the variable prevalence and recognition of subtle lesions is problematic. Reliable surgical data are small series not permitting multivariate analysis. Endometriosis is a hereditary disease. The oxidative stress of heavy menstrual bleeding with retrograde menstruation and an altered pelvic microbiome are probably associated with increasingly severe endometriosis. Whether the prevalence is increasing, or whether endometriosis is associated with fat intake or an increased risk of cardiovascular disease is unclear.



**Keywords**: Endometriosis; Epidemiology; Epigenetics; Genetics; Histology; Pathogenesis.

## 2 Plants as source of new therapies for endometriosis: a review of preclinical and clinical studies

Gabriela F Meresman, Martin Götte, Matthias W Laschke

**Abstract**

**Background**: Given the disadvantages and limitations of current endometriosis therapy, there is a progressive increase in studies focusing on plant-derived agents as a natural treatment option with the intention of achieving high efficiency, avoiding adverse effects and preserving the chance for successful pregnancy. The heterogeneity of these studies in terms of evaluated agents, applied approaches and outcomes illustrates the need for an up-to-date summary and critical view on this rapidly growing field in endometriosis research.

**Objective and rationale**: This review provides a comprehensive overview of plant-derived agents and natural treatment strategies that are under preclinical or clinical investigation and critically evaluates their potential for future endometriosis therapy.

**Search methods:** An English language PubMed literature search was performed using variations of the terms 'endometriosis', 'natural therapy', 'herb/herbal', 'plant', 'flavonoid', 'polyphenol', 'phytochemical', 'bioactive', 'Kampo' and 'Chinese medicine'. It included both animal and human studies. Moreover, the

Clinicaltrials.gov database was searched with the term 'endometriosis' for clinical trials on plant-derived agents. No restriction was set for the publication date.

Outcomes: Natural therapies can be assigned to three categories: (i) herbal extracts, (ii) specific plant-derived bioactive compounds and (iii) Chinese herbal medicine (CHM). Agents of the first category have been shown to exert anti-proliferative, anti-inflammatory, anti-angiogenic and anti-oxidant effects on

endometrial cells and endometriotic lesions. However, the existing evidence supporting their use in endometriosis therapy is quite limited. The most studied specific plant-derived bioactive compounds are resveratrol, epigallocatechin-3-gallate, curcumin, puerarin, ginsenosides, xanthohumol, 4-hydroxybenzyl alcohol, quercetin, apigenin, carnosic acid, rosmarinic acid, wogonin, baicalein, parthenolide, andrographolide and cannabinoids, with solid evidence about their inhibitory activity in experimental endometriosis models. Their mechanisms of action include pleiotropic effects on known signalling effectors: oestrogen receptor-α, cyclooxygenase-2, interleukin-1 and -6, tumour necrosis factor-α, intercellular adhesion molecule-1, vascular endothelial growth factor, nuclear factor-kappa B, matrix metalloproteinases as well as reactive oxygen species (ROS) and apoptosis-related proteins. Numerous studies suggest that treatment with CHM is a good choice for endometriosis management. Even under clinical conditions, this approach has already been shown to decrease the size of endometriotic lesions, alleviate chronic pelvic pain and reduce postoperative recurrence rates.

**Wider implications:** The necessity to manage endometriosis as a chronic disease highlights the importance of identifying novel and affordable long-term safety therapeutics. For this purpose, natural plant-derived agents represent promising candidates. Many of these agents exhibit a pleiotropic action profile, which simultaneously inhibits fundamental processes in the pathogenesis of endometriosis, such as proliferation, inflammation, ROS formation and angiogenesis. Hence, their inclusion into multimodal treatment concepts may essentially contribute to increase the therapeutic efficiency and reduce the side effects of future endometriosis therapy.

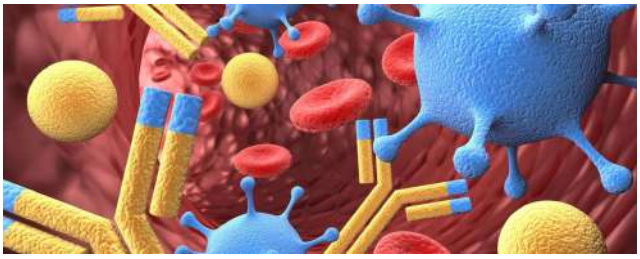
**Keywords**: Chinese herbal medicine; bioactive; endometriosis; flavonoid; herb; natural therapy; phytochemical; plant; polyphenol.

# 3 Endometriosis: What is the Influence of Immune Cells?

Paula Carolina Arvelos Crispim, MillenaPrataJammal, Eddie Fernando Candido Murta, RosekeilaSimõesNomelini

**Abstract**

**Background:** Endometriosis does not have a well-established physiopathology. It has been addressed that endometriosis is an inflammatory disease, where endocrine-immunological interactions are probably involved in the pathogenesis of the disease. The role of the immune system in endometriosis has been suggested to play an important role in both initiation and progression of the disease.Methods: A search for the following keywords was performed in the PubMed database: "endometriosis", "endometriosis and ovarian cancer", "endometriosis and immunology", and "endometriosis and cytokines".Results: The articles identified were published in English between 1921 and 2020. We selected 100 articles for further analysis.Conclusion: The recognition of the direct involvement of these two important physiological mechanisms causes a change in the pathophysiological focus of the disease. Researching the activities of numerous cells involved in immune reactions may offer new therapeutic targets.



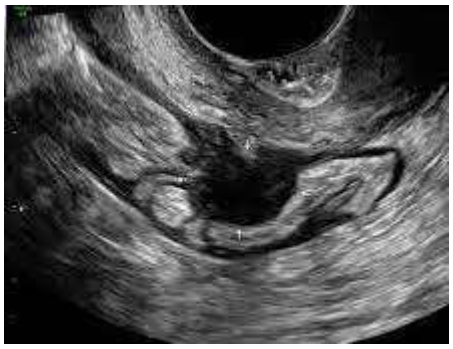
**Keywords:** Endometriosis; cytokines; immune cells; ovarian cancer.

# 4 Clinical and Sonographic Progression of Bowel Endometriosis: 3-Year Follow-up

Mauricio SimoesAbrao, Marina Paula Andres, Mariana da Cunha Vieira, Giuliano Moyses Borrelli, João SiufiNeto

**Abstract**

The aim of this study was to evaluate progression of the bowel endometriosis lesion over time. We performed a retrospective cohort with 164 patients with rectosigmoid endometriosis identified by transvaginal ultrasound (TVUS) with bowel preparation waiting for surgical treatment. Length and circumference of the bowel lesion evaluated by TVUS, painful symptoms (dysmenorrhea, dyspareunia, noncyclic pelvic pain, dyschezia, dysuria), and menopausal status were assessed at baseline and 6, 12, 24, 36, and > 36 months. A linear mixed model was used and p values < 0.05 were considered significant. We considered the length and the circumference as the main parameter; the characteristics were considered as fixed effects and the patient as random effect. This model allows to deal with missing data from longitudinal studies. All painful symptoms significantly improved during follow-up. Overall, the mean length and circumference of the greatest bowel lesion were 2.9 ± 1.8 cm and 27 ± 10%, respectively, and those did not change over time (p > 0.05). Patients with severe dyspareunia had significant greater circumference (p = 0.037) and those with severe dyschezia had significant greater length (p = 0.047) of bowel lesions. Symptoms were not related with progression of the lesion over time. The bowel lesion length significantly decreased over time in patients



in menopause (p = 0.009). There was no difference in the bowel lesion length between patients with and without hormonal treatment (p > 0.05). The results suggest that bowel endometriosis does not increase over time during reproductive age and reduces after menopause. Symptoms are also not related to the bowel lesion progression.

**Keywords**: Bowel endometriosis; Deep endometriosis; Disease progression; Hormonal treatment; Transvaginal ultrasound.

# 5 A Clinician's Guide to the Treatment of Endometriosis with Elagolix

Nicholas Leyland, Stephanie J Estes, Bruce A Lessey, Arnold P Advincula, Hugh S Taylor

**Abstract**

Pain associated with endometriosis is a considerable burden for women, permeating all aspects of their lives, from their ability to perform daily activities to their quality of life. Although there are many options for endometriosis-associated pain management, they are often limited by insufficient efficacy, inconvenient routes of administration, and/or intolerable side effects. Elagolix, a nonpeptide, small-molecule gonadotropin-releasing hormone (GnRH) receptor antagonist, is the first new oral therapy to be approved for the treatment of endometriosis-associated pain in the United States in more than a decade. Modulation of estradiol with elagolix is dose dependent and ranges from partial to full suppression. Clinical evidence has shown that elagolix at both approved doses (150 mg once daily and 200 mg twice daily) is effective for reducing symptoms of pelvic pain (dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia), improving quality of life, and decreasing use of rescue analgesics (nonsteroidal anti-inflammatory drugs and/or opioids). The availability of two dosing options allows for individualization of treatment based on


baseline clinical factors and response to therapy. Elagolix is well tolerated, with less pronounced hypoestrogenic effects compared with GnRH agonists. This review provides an overview of elagolix, highlighting currently available treatment options and the application of this new treatment for women with endometriosis-associated pain.

**Keywords**: GnRH receptor antagonist; dysmenorrhea; elagolix; endometriosis; pelvic pain.

# 6 Genetic analysis of endometriosis and depression identifies shared loci and implicates causal links with gastric mucosa abnormality

Emmanuel O Adewuyi, Divya Mehta, Yadav Sapkota, International Endogene Consortium; 23andMe Research Team; Asa Auta, Kosuke Yoshihara, Mette Nyegaard, Lyn R Griffiths, Grant W Montgomery, Daniel I Chasman, Dale R Nyholt

Evidence from observational studies indicates that endometriosis and depression often co-occur. However, conflicting evidence exists, and the etiology as well as biological mechanisms underlying their comorbidity remain unknown. Utilizing genome-wide association study (GWAS) data, we comprehensively assessed the relationship between endometriosis and depression. Single nucleotide polymorphism effect concordance analysis (SECA) found a significant genetic overlap between endometriosis and depression ($P_{Fsig\text{-}permuted} = 9.99 \times 10\text{-}4$). Linkage disequilibrium score regression (LDSC) analysis estimated a positive and highly significant genetic correlation between the two traits ($rG = 0.27$, $P = 8.85 \times 10\text{-}27$). A meta-analysis of endometriosis and depression GWAS (sample size = 709,111), identified 20 independent genome-wide significant loci ($P < 5 \times 10\text{-}8$), of which eight are novel. Mendelian randomization analysis (MR) suggests a causal effect of depression on endometriosis. Combining gene-based association results across endometriosis and depression GWAS, we identified 22 genes with a genome-wide significant Fisher's combined P value ($FCPgene < 2.75 \times 10\text{-}6$). Genes with a nominal gene-based association ($Pgene < 0.05$) were significantly enriched across endometriosis and depression ($Pbinomial\text{-}test = 2.90 \times 10\text{-}4$). Also, genes overlapping the two traits at $Pgene < 0.1$ ($Pbinomial\text{-}test = 1.31 \times 10\text{-}5$) were

significantly enriched for the biological pathways 'cell-cell adhesion', 'inositol phosphate metabolism', 'Hippo-Merlin signaling dysregulation' and 'gastric mucosa abnormality'. These results reveal a shared genetic etiology for endometriosis and depression. Indeed, additional analyses found evidence of a causal association between each of endometriosis and depression and at least one abnormal condition of gastric mucosa. Our study confirms the comorbidity of endometriosis and depression, implicates links with gastric mucosa abnormalities in their causal pathways and reveals potential therapeutic targets for further investigation.

# B NEWS FROM OUR SOCIETY
## PAST ACTIVITIES

### @endometriozis_tr Live Streams

In the past three months during whichthe pandemic still affected us, we continued live broadcasts on our Instagram account to connect with our patients and answer their valuable questions. Here is the list of our broadcasts:


**Q&A 22: Everything about endometriosis**
Prof. Taner Usta, MD.
Karolin Ohanoglu , MD.


**Q&A 23: Everything about endometriosis**
Prof. Cem Atabekoglu, MD.
Aysegul Mut, MD.


**Q&A 24: Everything about endometriosis**
Prof. Umit Inceboz, MD.
Isik Sozen, MD.


**Q&A 25: Everything about endometriosis**
Assoc. Prof. Omer Lutfi Tapisiz, MD.
Sebnem Alanya Tosun, MD.


**Q&A 26: Everything about endometriosis**
Prof. Murat Ulukus, MD.
Humeyra Demirkiran, MD.


**Q&A 27: Everything about endometriosis**
Prof. Gazi Yıldırım, MD.
Assoc. Prof. Yusuf Aytac Tohma, MD.


**Q&A 28: Everything about endometriosis**
Prof. Husnu Gorgen, MD.
Goknur Topcu, MD.

## Turkish Endometriosis & Adenomyosis Society Webinars 2021

The webinar series continued with **'Endometriosis and Adverse Perinatal Outcomes: An Update 2021'** on April 27, 2021. It was moderated by **Dr. Levent Senturk** and **Dr. Ibrahim Bildirici**. **Dr. Recai Pabuccu** and **Dr. Baris Mulayim** shared their knowledge and experiences.

Our second webinar, **'Diagnosis of Endometriosis 2021: An Update'**, which was moderated by **Dr. Timur Gurgan** and **Dr. Yaprak Ustun** was held on the 25th of May. **Dr. Sebastian Schafer** from Germany, **Dr. Gaby Moawad** from USA and **Dr. Pinar Yalcin Bahat** from Turkey shared their experiences.


**8- Endometriosis and Adverse Perinatal Outcomes: An Update 2021**

Moderators: **Levent Senturk, MD.**
**Ibrahim Bildirici, MD.**

Speakers: **Recai Pabuccu, MD.**
**Baris Mulayim, MD.**


**9- Diagnosis of Endometriosis 2021: An Update**

Moderators: **Timur Gurgan, MD.**
**Yaprak Ustun, MD.**

Speakers: **Sebastian Schafer , MD.**
**Gaby Moawad, MD.**
**Pinar Yalcin Bahat, MD.**

## 9th National Gynecologic Endoscopy Congress and 3rd Young Endoscopists Symposium

**Pelvic Pain Workshop**

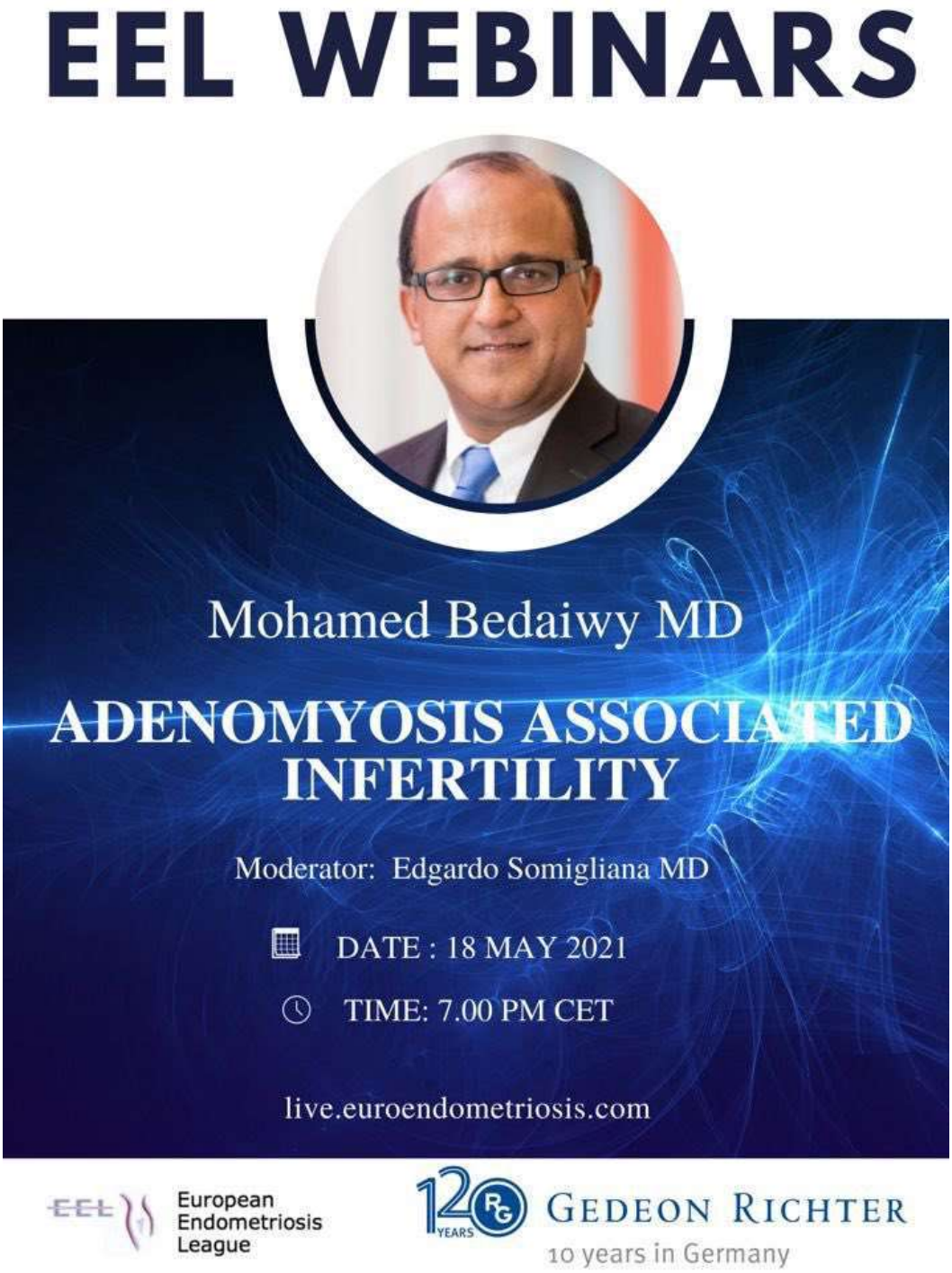
After a long pause to the face-to-face meetings due to the pandemic, the pre-congress Pelvic Pain Workshop was successfully carried out on site organized by Prof. Taner Usta, MD and Prof. Ahmet Kale, MD at Istanbul Kartal Dr. Lutfi Kirdar City Hospital, Members of our board of directors and different specialist dealing with chronic pelvic pain attended the meeting.

# C NEWS FROM THE WORLD OF ENDOMETRIOSIS

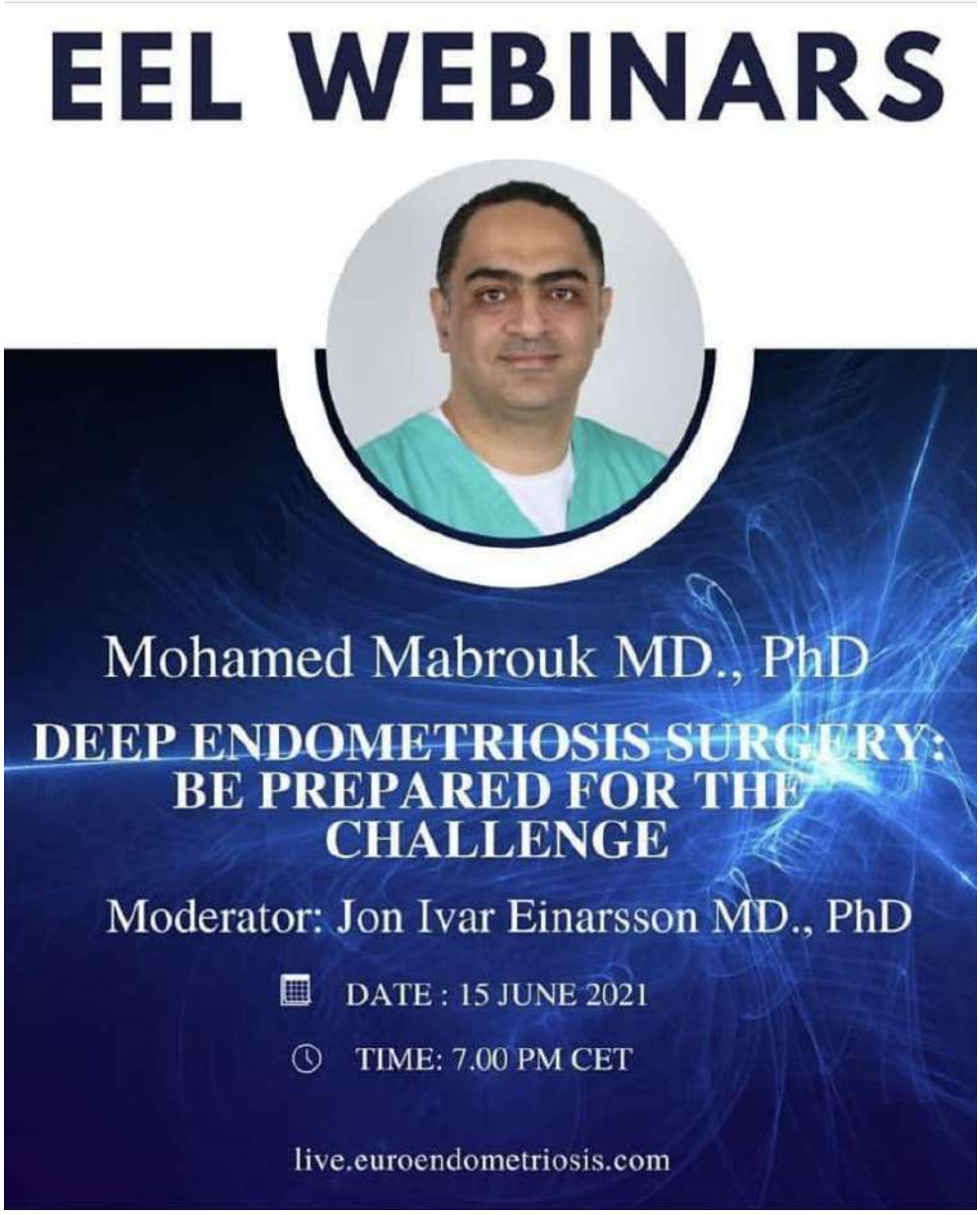
## EEL WEBINAR Program 2021

In the first EEL Webinar held in April, with the title 'Navigation in the Labyrinth of Parametrial Endometriosis: From Accurate Diagnosis to Proper Surgical Management', Dr. Mario Malzoni described the management of endometriosis with parametrial involvement.

The EEL Webinar held in May with the title of 'Adenomyosis Associated Infertility' was presented by Dr. Mohamed Bedaiwy.



The EEL webinars continued with a comprehensive presentation held in June, titled 'Deep Endometriosis Surgery: Be prepared for the challenge' by Dr. Mohamed Mabrouk.



European Endometriosis League (EEL) Webinar programs continue in 2021 as well.

In the webinar program, which is planned to be held every month, international physicians experienced in endometriosis will share their knowledge on different subjects. For more information, visit htthttps://www.endometriosis-league.eu/home or follow the European Endometriosis League or Euro Endo League accounts on social media.

## ESHRE 2021


37th annual meeting of ESHRE (European Society of Human Reproduction and Embryology) was held on 27-30th of June, 2021.

## Endometriosis 2021-Roma

Endometriosis 2021 meeting which was postponed due to the COVID-19 pandemic, was held online on May 8-11, 2021.

## ACE2021


9th Asian Conference on Endometriosis organized by Sri Lanka Endometriosis Society and Asian Society of Endometriosis and Adenomyosis and The Endometriosis and Adenomyosis Association of Sri Lanka was postponed to October 28-30, 2021 due to the pandemic.

## 6th EEL Congress-France


The 6th EEL Congress is planned to be held in Bordeaux, France, in December this year. Our colleagues interested in the subject may attend this meeting, which will bechaired by Horace Roman who is especially experienced in deep infiltrative endometriosis.

## AAGL 2021


The 50th Global Congress of Minimally Invasive Gynecological Surgery (MIGS) by AAGL is planned to be held on 14-17 November 2021 in Austin Texas, USA.

## SEUD 2021


The 7th Congress of Endometriosis and Uterine Pathologies is planned to be held in Stockholm, Sweden in December this year.

## FIGO 2021


World Congress of Gynecology and Obstetrics (FIGO) is going to be held in Sydney, Australia.

# D INTERVIEW WITH AN 'ENDO SPECIALIST'

**Lone Hummelshoj**
**Interviewer: Assoc. Prof. Hale Goksever Celik, MD**

## A Short Curriculum Vitae

Lone Hummelshoj has been chief executive at the World Endometriosis Society (WES) since 2005. She is responsible for the implementation of WES' strategic plan, including endometriosis world congresses. In addition to her roles at WES, Lone is the publisher/chief editor of www.endometriosis.org, a global forum for endometriosis-related news and information. She is also the executive director of the World Endometriosis Research Foundation andan active member of the ESHRE, AAGL and ASRM Special Interest Groups on Endometriosis. She has authored articles and chapters in more than 45 peer-reviewed journals on endometriosis. (H-index = 31).

**Turkish Endometriosis & Adenomyosis Society (EAD):** Hello Lone, welcome! Thank you for being here for this interview.

**Lone Hummelshoj:** Hello! How are you?

**EAD: I'm fine, thank you very much. How are you?**

**LH**: I'm fine too, thank you.

**EAD: Thank you very much for accepting our interview offer. This interview will take an average of 30 minutes. I hope you are in good health after vaccination.**

**LH**: Ah yes! Yes, I am fine, thank you very much.

**EAD: First of all, I would like to introduce myself. I work as an associate professor in the department of obstetrics and gynecology at a university in Istanbul. I have been a member of the Turkish Endometriosis and Adenomyosis Society since 2017 and you know that I have been the Turkey representative of the World Endometriosis Association since 2019. We work on endometriosis and adenomyosis and try to raise awareness for both patients and clinicians. I have prepared some questions for you. If you're ready, shall we begin?**

**LH:** Sure.

**EAD: We, as the Turkish Endometriosis and Adenomyosis Society, publish a quarterly newsletter. Also, we're interviewing endometriosis and adenomyosis experts, like you. Can you tell us about your contributions to the field of endometriosis?**

**LH:** That's a pretty long story. I honestly don't know where to start. In 1997, I became one of the founders of the Danish Endometriosis Society. I took part in the project management of the first ESHRE directive on endometriosis. I took place as chief executive in 2005 and became one of the co-founders in 2008. Frankly, I do not know exactly how many project managements I took part in workshops, reconciliation, meetings and collaborative activities. In 2005, I was on the organizing committee of the World Endometriosis Congress. I took part in the congresses in 2008, 2011, 2014, 2017, 2021 as an auditor and now I will take part in the congress in 2023 in the same way.

**EAD: When and how did you decide to work in the field of endometriosis?**

**LH:** I have severe endometriosis myself. That's why I joined the Danish Endometriosis Society.

**EAD: You are in contact with many endometriosis patients through the association. Have you ever met a patient with a different story that impressed you?**

**LH:** I think it did, there was a group of young women who really impressed me. They had spent years looking for someone to listen to them. People had told them that the pain was not real and had been in their head for years. However, they said that the pain destroyed them, prevented them from going to school, and ruined their relationships. Quite a long time later, they were diagnosed with severe endometriosis. I think that impressed me the most.

**EAD: Thank you very much. We know that there are many patients who cannot be diagnosed with endometriosis. We also know that these people are delayed by an average of 10 years in diagnosis because there are currently no non-invasive diagnostic markers. As the chief executive of the World Endometriosis Society, can you tell me how many women on average have endometriosis in the world?**

**LH:** No, I can't say precisely, because nobody knows this. But we know that roughly 10% of women between 15-50 years have complaints of infertility, menopause, pain, and endometriosis may be the cause. This 10% should be roughly 190 million people, I guess.

**EAD: Yes, we know that this frequency increases in infertile patients and reaches approximately 40%. What advice would you like to give these patients about coping with endometriosis?**

**LH:** In dealing with endometriosis, they should always insist on seeing a gynecologist who specializes in the treatment of endometriosis. And they must always insist that all treatment options are available. It should not be spoken of as “you must take this medicine” or “you must have this surgery”. They should be informed that there are various options for treatment. Explanations such as “this drug has these side effects”, “this surgery has these risks” should be made. So, all options should be offered to these women. I would also say that they can seek advice from other women with endometriosis. Each case is individual. A treatment that works for one person may not work for another but sharing experiences can sometimes help. For example, tips such as “you need to get enough rest”, “you need to eat regularly” may work.

**EAD: In Denmark, you worked with politicians to help change national referral guidelines. This facilitated the referral of patients with endometriosis to a national center specialized in the treatment of endometriosis. Can you briefly describe how you achieved this?**

**LH:** That was over 20 years ago. I called the Danish Minister of Health secretary and requested a meeting and he accepted. I took a gynecology professor from Aarhus University with me to this meeting with the Minister of Health. In the meeting, we talked about the impact of this disease on women's quality of life, its impact on school life, delays in diagnosis and mistreatment. We didn't have the numbers 20 years ago. Therefore, we had to make some assumptions. But he understood what we were trying to tell him. At that time, it was believed that only cancer required special treatment. Similar to other conditions such as preeclampsia which has to be treated by specialists, endometriosis has to be treated by a specialist as well. Thus, estimates were made about the portion of the Danish population that had endometriosis. The decisions taken were quickly implemented with the National Institute of Health about a year later, and they have been implemented for 20 years.

**EAD: You have made various presentations on the impact of endometriosis and the need for patient-based care centers by attending various international meetings in Europe, America, Africa and Asia. You have also established patient support and donation platforms by working with national groups. Can you tell us a little about your experiences during this time? treat**

**LH**: I've seen endometriosis act on women the same way around the world. All women suffer from endometriosis in the same way. In other words, this disease does not discriminate according to whether the skin color is white, black or dark. It doesn't discriminate based on what your hair color is, or whether you're overweight or thin. This disease affects everyone the same way who are unlucky enough to have it. At the same time, I learned that those who really want to make a difference can do something to improve endometriosis care, and that's what makes the difference worldwide. Differences will arise depending on the extent to which clinicians and scientists specializing in this particular field are involved in a country. We can see good examples of websites on endometriosis and pain in countries such as Australia, New Zealand, Denmark and England. Several endometriosis organizations worldwide that include national support groups, research branches, clinicians and scientists who want to do research on endometriosis, meet at one of the universities every year and spend the whole day together organizing the distribution of tasks for each group. Collaboration is the most important thing for me, because in endometriosis there are no orders. So, I think we need to cooperate more than ever before.

**EAD: Collaboration is important.**

**LH:** Absolutely important.

**EAD: We know you worked hard and got endometriosis on the European commission's 2006 working agenda and then funded an endometriosis project through the Public Health Program in May 2007. Can you tell us what kind of contributions these projects have made to the lives of endometriosis patients?**

**LH: I**t's hard to say because all the projects took quite a long time. But if you ask "what happened when we put endometriosis on the study agenda?" I can say that it has created hope that endometriosis projects can be accepted and supported. There are two projects that I know of, one of them is the "IMI pain project (IMI-paincare)" which also includes bladder pain. However, it is mainly a project related to endometriosis-induced pain. This project is also a giant project supported by industry partners. The other is the "Female" project and is supported by a high amount of 6 million Euros. This project is only about endometriosis. It is supported by several clinics, universities and companies across Europe, including Switzerland, Hungary, France, England. It is also supported by Aarhus University in Denmark. I also took part in this project as a part of the application software.

**EAD: You've been running your own business development consulting firm from London, UK, where you specialize in business development, strategic marketing, project management and facilitation since 1996. How did you decide to do this?**

**LH:** This is my job as a freelancer. But I always work on endometriosis. In other words, I also do strategic marketing in the field of endometriosis. I'm doing this for the World Endometriosis Society. I manage projects.I am a business development specialist. But I can do this for every company in the same way. But I don't have enough time to do this for everyone.

**EAD: Finally, do you have any message you would like to convey to endometriosis patients and physicians?**

**LH:** Listen to each other. Communication and collaboration are the keywords here. The doctor should take the time to listen to his patient. Because the patient is trying to tell what went wrong. Nobody goes to the doctor to tease or distract the doctor. No one has time to do this. So, if the patient is there, it's because something isn't right. Listen to her. And then I'll say the same thing to the patient. You should listen to your doctor. If you have endometriosis, you should consult a doctor who specializes in this area. If not, you should request referral to a specialist and listen to the treatment options available to you. You have to decide what is the best solution for you. As I said before, you should talk to other people who have the disease. But you shouldn't let the person you're talking to tell you what's best for you. Because only you can know what's best for you.

**EAD: Yes, you are right. I work in a public hospital and can only spare ten minutes for each patient. I especially try to spare about 30 minutes for endometriosis patients. Because these patients cannot explain some symptoms quickly and I have to ask one by one "Do you have pain in the pelvic region, do you have pain during sexual intercourse, do you have a complaint of painful menstruation". You are right, it is important to listen and take time for these patients.**

**LH:** You may be the first doctor to say you listened to them. This made me happy. I'm happy to know that someone was listening to them. It created a sense of trust. There is so much to say.

**EAD: Yes. I operated on a patient with endometriosis yesterday. She was discharged today. It was enough for her to stay in the hospital for one day. She felt extremely well after the surgery. I explained every single detail face to face. I explained all the treatment options before and after the surgery. So, listening and communication between patient and doctor is important. I agree with you on this and thank you very much.**

**LH:** I am very pleased. I wish you success on your article.

**EAD: Thank you very much. Prof. Dr. Engin Oral and Prof. Dr.TanerUsta conveyed their greetings to you. Thank you so much.**

**LH:** Please pass on my best wishes to them and keep working.

**EAD: Thank you very much.**

**LH:** Thank you very much for everything you do. I am very pleased.

**EAD: I would love to collaborate on future projects as well.**

**LH:** I would be very happy.

**EAD: Thank you very much, good evening.**

# E ARTICLES ON ENDOMETRIOSIS FROM OUR COUNTRY FROM THE LAST THREE MONTHS

### 1. Assisted reproductive technology for women with endometriosis, a clinically oriented review

Baris Ata 1, Savci Bekir Telek 2 Current Opinion in Obstetrics and Gynecology 2021; Jun 1;33(3):225-231. doi: 10.1097/GCO.0000000000000710.

**Abstract**

**Purpose of review:** To discuss optimal management of an assisted reproductive technology (ART) cycle in women with endometriosis.
Recent findings: New studies involving euploid embryo transfers provide more insight on the etiology of endometriosis-associated infertility. Oocyte competence to reach live birth seems unlikely to be affected by the disease. Routine medical or surgical treatment prior to an ART cycle does not appear beneficial. Short gonadotropin releasing hormone (GnRH) antagonist or progestin primed ovarian stimulation protocols seem to be proper first choices, depending on the intention for a fresh embryo transfer. Low-quality evidence supports frozen thawed over fresh embryo transfer. Ovarian stimulation for ART does not seem to be associated with symptom progression or recurrence.

**Summary**: How endometriosis affects fertility is still unclear, but ART is an effective pragmatic treatment. Each woman with endometriosis must be assessed with a holistic approach, and in the absence of an indication for otherwise, ART cycles can be kept simple with patient-friendly protocols. Whether a frozen embryo transfer is better than a fresh one should be investigated.

**Keywords**: assisted reproduction , endometrioma , endometriosis , ovarian stimulation , progestin

### 2. Uterine involvement by endometriosis: Sonographic features from elusive findings to apparent adenomyosis

Safak Olgan 1, Enver Kerem Dirican 2, Arif Can Ozsipahi 2, Mehmet Sakinci 2 European Journal of Obstetrics & Gynecology Reproductive Biology 2021 May 9;262:93-98. doi: 10.1016/j.ejogrb.2021.05.013

**Abstract**

**Objective:** The primary aim of this study is to investigate whether there are any minor sonographic uterine findings, not typical for adenomyosis, in endometriosis patients. The secondary objective is to determine the prevalence of sonographic features of adenomyosis in an infertile population with endometriosis.

**Study design:** The investigation was of 291 infertile women with endometriosis, either manifesting endometrioma (OMA) or diagnosed through laparoscopy, who were investigated for two-dimensional transvaginal sonographic (2D-TVS) features of adenomyosis. These patients were grouped as either having endometriosis with adenomyosis (EwA,n = 121) or without adenomyosis (EwoA, n = 170). Additionally, patients without both endometriosis and 2D-TVS features of adenomyosis constituted the control group (n = 170).

**Results:** At least one 2D-TVS feature of adenomyosis was detected in 41.6 % (n = 121) of women with endometriosis. Asymmetrical myometrial thickening of uterine walls (57.9 %), hyperechogenic islands (47.1 %), and fan-shaped shadowing (46.9 %) were relatively more prevalent 2D-TVS findings among EwA patients. Multiple OMA (p = 0.038), OMA ≥ 4 cm (p = 0.034), and total OMA volumes were found to be higher (p = 0.004) in the EwA group. Additionally, uterine volumes were found to be 96.7 cm3, 73.0 cm3, and 64.2 cm3 in the EwA, EwoA, and control groups, respectively (EwA vs EwoA, p < 0.001; EwoA vs control, p <0.001). Multivariate linear regression analysis revealed that the presence of endometriosis was independently associated with an increase in uterine volume (β = 0.243, p < 0.001).

**Conclusion:** A stepwise and statistically significant volume increase from the control group to the EwoA and then to the EwA group may reflect a spectrum of uterine involvement in endometriosis. This might indicate that many uterine endometriosis cases are still hidden from view, possibly demonstrating an "iceberg phenomenon".

**Keywords:** Adenomyosis; Endometriosis; Uterine endometriosis; Uterine volume.

### 3. Circulating serum miR-200c and miR-34a-5p as diagnostic biomarkers for endometriosis

Sema Misir 1, Ceylan Hepokur 2, Bugra Oksasoglu 3, Caglar Yildiz 4, Ali Yanik 4, Yüksel Aliyazicioglu 5 Journal of Gynecology Obstetrics and Human Reproduction 2021 Apr;50(4):102092. doi: 10.1016/j.jogoh.2021.102092.Epub 2021 Feb 15.

**Abstract**

**Objective:** Endometriosis is defined by the presence of endometrial glands and stroma grow in areas outside the uterus. A simple blood test for endometriosis-specific biomarkers would offer a more timely accurate diagnosis of the disease and could lead to earlier treatment intervention. Alterations in microRNA (miRNA) levels in blood may reflect changes during normal physiologic processes and have been related to several pathologic conditions, including gynecologic diseases. In the present study, we aim to evaluate the level of serum miR-34a-5p and miR-200c from women with and without endometriosis, and to explore the potential of miRNAs as reliable non-invasive biomarkers in the diagnosis of endometriosis.

**Methods**: Expression levels of miRNAs were performed by quantitative real-time polymerase chain reaction (qRT-PCR). Serum cancer antigen 125 (CA-125) levels were analyzed by autoanalyzer.

**Results**: miR-34a-5p expression levels were decreased and miR-200c expression levels were increased in the endometriosis patients compared to the control group. According to the areas under the ROC curve (AUC) values, miR-200c and miR-34a-5p may serve as biomarkers for the diagnosis of endometriosis. Serum miR-34a-5p and miR-200c had a sensitivity of 78.95 % and 100 % and a specificity of 49.12 % and 100 %, respectively, for the detection of endometriosis.

**Conclusion**: Serum miRNAs may provide a promising opportunity for diagnosis of endometriosis. Understanding the role of circulating miRNAs will serve a better comprehension of the systemic effects of endometriosis and offer options for new treatments. It is clear that more work is needed in this area.

**Keywords**: Biomarker; Endometriosis; Non-invasive diagnosis; miR-200c; miR-34a-5p.

### 4. Are women with small endometriomas who undergo intracytoplasmic sperm injection at an elevated risk for adverse pregnancy, obstetric, and neonatal outcomes?

Fatma Ferda Verit 1, Ayse Seyma Ozsuer Kucukakca 2 Clinical and Experimental Reproductive Medicine 2021 Mar;48(1):80-84. doi: 10.5653/cerm.2020.03776. Epub 2021 Feb 18.

**Abstract**

**Objective**: The aim of the study was to investigate pregnancy, obstetric, and neonatal outcomes in women with small (<4 cm) unilateral endometriomas.

**Methods**: This retrospective study included 177 patients: 91 patients with small endometriomas and 86 controls with unexplained or tubal factor infertility who were treated at the Süleymaniye Gynecology and Maternity Training and Research Hospital Infertility Unit between January 2010 and July 2015. The groups were matched with regards to demographic characteristics such as age, body mass index, and infertility duration. All of the women in this study conceived via intracytoplasmic sperm injection. We compared pregnancy, obstetric, and neonatal outcomes between these groups.

**Results**: Women with endometriomas had a higher biochemical pregnancy rate, but lower clinical pregnancy and live birth rates than women with unexplained and tubal factor infertility ($p<0.05$ for all). However no significant differences were found in terms of obstetric and neonatal complications between the two groups ($p>0.05$ for all).

**Conclusion**: In this study, we found that women with endometriomas less than 4 cm were more prone to early pregnancy complications. We also showed that this group did not have any increased risks of late pregnancy, obstetric, and neonatal complications.

**Keywords**: Endometrioma; Neonatal; Obstetric outcome; Pregnancy.

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