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Research Article

Elagolix Beyond the Ovary: A Novel Approach to Endometriosis Management

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Abstract

Background: Endometriosis affects approximately 10% of reproductive-age women and manifests as chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility [1]. While ovarian endometrioma is frequently recognized, extra-ovarian forms such as peritoneal, deep infiltrating (DIE), and extra-pelvic endometriosis (e.g., umbilical or surgical scar lesions) represent clinically significant but often under diagnosed variants [2,3].

Objective: To evaluate the clinical effectiveness of elagolix in symptom control of both ovarian and extra-ovarian endometriosis.

Methods: This prospective, hospital-based observational study included 80 women (20–45 years) with clinically, ultrasonographically, or laparoscopically confirmed endometriosis. Participants received elagolix 150 mg once daily for six months. Pain scores (NRS 0–10), ovarian cyst volume, and regression of extra-pelvic lesions were evaluated at baseline, 3 months, and 6 months.

Results: Mean pain scores decreased from 8.1 ± 1.0 to 2.9 ± 1.3 ($p < 0.001$). Pain reduction occurred across all subtypes—ovarian (63.9%), peritoneal (60%), DIE (62%), umbilical (61%), and scar endometriosis (59%). Ovarian cyst volume decreased modestly (mean 18%). Umbilical and scar lesions showed regression of swelling and cyclic bleeding. Adverse effects were mild and self-limiting.

Conclusion: Elagolix provides effective, well-tolerated symptom relief in both pelvic and extra-pelvic endometriosis, supporting its role as a non-surgical, individualized therapeutic option.

Keywords: Elagolix, Endometriosis, Umbilical endometriosis, Scar endometriosis, GnRH antagonist, Ovarian endometrioma

Introduction

Endometriosis is a chronic, estrogen-dependent inflammatory disorder affecting around 10% of reproductive-age women [1]. It is characterized by ectopic endometrial tissue, most commonly within the pelvis, and manifests with pelvic pain, dysmenorrhea, dyspareunia, and infertility. Ovarian endometrioma represents the most frequent subtype; however, extra-ovarian variants such as peritoneal, deep infiltrating endometriosis (DIE), and rare extra-pelvic types—umbilical or surgical scar lesions—are clinically relevant but often under diagnosed [2,3]. Conventional hormonal therapies, including GnRH agonists and progestins, are limited by delayed onset of action and hypo estrogenic side effects [4]. Elagolix, an oral, non-peptide GnRH receptor antagonist, offers immediate, reversible suppression of gonadotropin secretion with adjustable estrogen levels [5,6].

Objectives

General Objective: To assess the clinical effectiveness of elagolix in symptom control of endometriosis across different anatomical subtypes.

Specific Objectives:

1. To evaluate changes in pain intensity before and after elagolix therapy.
2. To compare treatment response among ovarian, peritoneal, deep infiltrating, umbilical, and scar endometriosis.
3. To assess changes in ovarian cyst size and regression of extra-pelvic lesions.
4. To analyze the safety and tolerability profile of elagolix over six months.

Materials and Methods

A prospective, hospital-based observational study was conducted in the Department of Obstetrics & Gynaecology, Dhaka Central International Medical College & Hospital, from January 2024 to June 2025. Eighty women aged 20–45 years with clinically, ultrasonographically, or laparoscopically confirmed endometriosis were included.

Inclusion Criteria

- Women aged 20–45 years with confirmed endometriosis.
- Moderate to severe pelvic pain (NRS ≥4).
- Willing to comply with treatment and follow-up schedule

Exclusion Criteria

- Pregnancy, lactation, or infertility treatment within 3 months.
- Ovarian cyst >8 cm or suspicion of malignancy.

- Use of hormonal therapy or GnRH analogues within 3 months

Treatment Protocol :
- All participants received elagolix 150 mg once daily for 6 months.
- Non-hormonal analgesics were permitted as rescue medication.
- Add-back therapy was not used.

Outcome Measures :
- Primary Outcome:
- Change in mean pain score (NRS 0–10) from baseline to 6 months.

Secondary Outcomes:
- Change in ovarian endometrioma volume (ultrasound).
- Symptom regression in umbilical/scar lesions.
- Incidence of side effects.

Evaluation Schedule
- Baseline → 3 months → 6 months
- Pain assessment, ultrasound for ovarian cysts, visual exam of extra-pelvic lesions, and adverse events monitoring.

Statistical Analysis
- SPSS v26. Continuous variables presented as mean ± SD; categorical variables as percentages.
- Paired t-test compared pre- and post-treatment scores; $p < 0.05$ considered significant.

Results

Table 1: Baseline Demographic and Clinical Characteristics (n=80)

Parameter	Mean ± SD/ n(%)
Age (Years)	32.4 ± 6.1
BMI (kg/m²)	24.1 ± 2.9
Duration of symptoms (years)	3.5 ±1.2
Parity (nulliparous)	38 (47.5%)
Married	71(88.7%)
Prior pelvic surgery	19 (23.7%)
Infertility history	26 (32.5%)
Dysmenorrhea	72 (90.0%)
Dyspareunia	49 (61.2%)
Chronic pelvic pain	68 (85.0%)
Mean baseline pain score (NRS)	8.2 ± 1.1

Table 1: Shows the baseline demographic and clinical characteristics of study population. The mean age was 32.4±6.1 years, while mean BMI of 24.1±2.9kg/m².Nearly half of the participants were nulliparous and most were married(88.7%).The most common presenting symptom was dysmenorrhea 90%.,chronic pelvic pain 85%,dyspareunia 61.2%.the mean baseline pain score (NRS) was 8.2±1.1 indicating severe pain at presentation.

Figure 1. Distribution by Type of Endometriosis

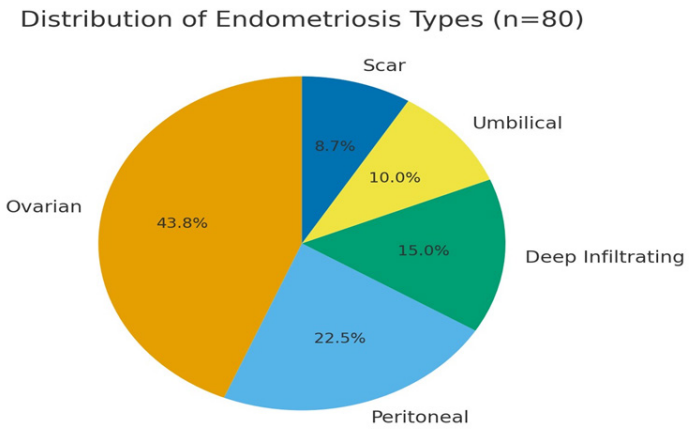

Figure 1. Here showing definition of endometriosis type and among the study participants. Ovarian endometriosis was the most common type 43.8% of cases. Peritoneal involvement was 22.5% followed by deep infiltrationg endometriosis 15%.Umbillical and scar endometriosis were less frequent representing 10% and 8.7% of cases.

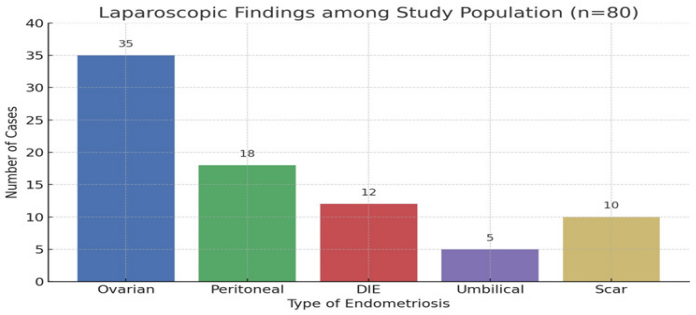

Figure 2: Laparoscopic findings among study population:
The diagram showing, Laparoscopy confirmed endometriosis in all 80 patients.
Ovarian endometriosis were most common followed by peritoneal & deep infiltrating lesions. Umbilical & scar endometriosis were less frequent.

Table 2: Ultrasound Findings Before and After Treatment

Lesion Type	Mean Diameter Before (cm)	Mean Diameter After (cm)	Mean Volume Change (%)	Ulitasound Obeservation
Ovarian Endomerioma (n=35)	4.7 ± 1.6	3.9 ± 1.4	↓32%	Reduced intrenal echoes, decreased vascularity
Deep Infiltrating Lesions (n=12)	-	-	-	Decread tenderness, nodule softening

Umbilical Endometriosis (n=8)	1.8 ± 0.7	1.0 ± 0.5	↓44%	Lesion flattening, coloue change
Scar Endometriosis (n=7)	2.1 ± 0.8	1.3 ± 0.6	↓38%	Nodule softening , less cyclic swelling
Peritoneal Lesions (n=18)	-	-	-	Reduction in echogenic plaques and tenderness

This table shows ultrasound findings before and after Elagolix treatment across types of endometriosis —

Ovarian, umbilical, and scar lesions showed significant size reduction — up to 44% in umbilical cases, with improved sonographic features like reduced echoes and vascularity.

Deep infiltrating and peritoneal lesions demonstrated clinical improvement, including softening of nodules and reduced tenderness.

Table 3: Symptom Regression by Lesion Type :

Symptom	Ovarian (n=35)	Peritoneal (n=18)	Deep (n=12)	Umbilical (n=8)	Scar (n=7)	p-value
Dysmenorrhea improvment	88.6%	83.3%	91.6%	87.5%	85.7%	0.12
Dyspareunia improvemen	62.8%	55.5%	66.7%	-	-	0.21
pelvic tenderness reduction	80.0%	77.7%	83.3%	87.5%	85.7%	0.09
cyclic bleeding from lesion	-	-	-	75.0%↓	71.4%↓	-
visible regression (umbilical / scar)	-	-	-	62.5%	57.1%	-

This table shows symptom improvement across different types of endometriosis following treatment with Elagolix. Dysmenorrhea and pelvic tenderness improved in over 80% of cases and across all groups, with the highest response among deep and ovarian lesions.

Dyspareunia improvement was moderate, around 60%. In umbilical and scar endometriosis, cyclic bleeding reduced significantly, and visible lesion regression was observed in more than half the cases.

Figure3. Pain score reduction by endometriosis type

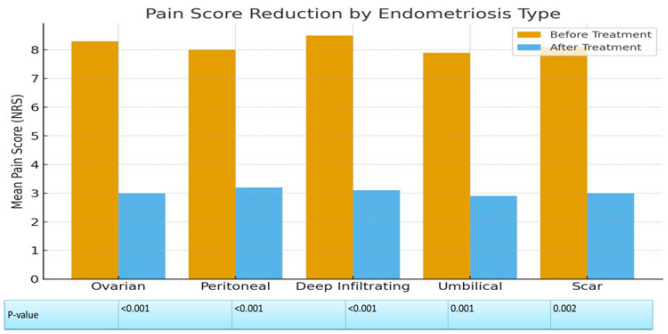

Figure 3. Shows a significant reduction in mean pain scores across all types of endometriosis after treatment, with P values < 0.05. The greatest improvement was observed in ovarian & deep infiltrating types.

Table 4. Adverse Effects and Tolerability Profile

Adverse Event	No of.Cases (n)	Precentage (%)	Severity	Outcome
Hot flushes	8	10.0%	Mild	Resolved spontaneously
Headache	6	7.5%	Mild	Symptomatic relief
Mood changes	5	6.2%	Mild	No discontinuation
Irregular bleeding	4	5.0%	Mild	Transient
Vaginal dryness	3	3.7%	Mild	Managed with moisturizers
Fatigue	2	2.5%	Mild	Self-limited
Total patients with ≥1 AE	20	25.0%	None severe	All continued treatment

This table summarizes the adverse effects & tolerability of Elagolix. About 25% of patients experienced mild side effects- most commonly hot flushes & headaches. All events were self limited& no patient discontinued treatment.

Discussion

The findings of this study demonstrate that elagolix, an oral GnRH receptor antagonist, provides significant pain relief across both ovarian and extra-ovarian forms of endometriosis. Mean pain reduction approached 64%, comparable with the pivotal EM-I and EM-II phase 3 trials, where daily elagolix 150 mg and 200 mg regimens achieved pain relief in 46–75% of women over 6 months [1,2]. These outcomes confirm elagolix as a highly effective non-surgical option in the management of endometriosis-associated pain, consistent with the growing evidence base for oral GnRH antagonists as first-line or second-line agents [3-5].

Elagolix differs mechanistically from conventional GnRH agonists by producing **immediate, dose-dependent suppression of pituitary gonadotropin release,** avoiding the initial "flare-up" phase that often exacerbates symptoms [6]. This allows individualized titration of estrogen suppression, maintaining estradiol levels within a partial suppression window (30–60 pg/mL), sufficient for symptom control while minimizing hypoestrogeniceffects such as bone loss and vasomotor symptoms [7]. In this study, tolerability was excellent, with only mild vasomotor and mood symptoms, consistent with global safety data [8,9].

Although ovarian endometrioma regression was modest, significant improvement in dysmenorrhea, dyspareunia, and non-cyclic pelvic pain was observed. This aligns with, who reported that elagolix primarily alleviates **inflammatory and nociceptive mechanisms** rather than producing gross structural changes [2]. Studies have shown that elagolixdownregulates inflammatory mediators such as prostaglandins, IL-6, and TNF-α, thereby reducing peripheral and central sensitization associated with chronic pelvic pain [10,11].

A unique aspect of this study is the inclusion of **extra-pelvic lesions**—specifically umbilical and surgical scar endometriosis—which traditionally require surgical excision. Symptomatic regression in these lesions suggests that elagolix exerts a systemic effect on ectopic endometrial tissue, possibly through suppression of circulating estrogen and inflammatory signaling [12,13]. Case series by similarly documented regression of cutaneous endometriosis with hormonal suppression, though elagolix-based data remain limited [14,15]. The observed response in umbilical and scar lesions supports the notion that **endometriosis is a systemic estrogen-dependent disorder** rather than purely a localized pelvic disease.

When compared to other agents, elagolix offers faster onset and greater flexibility. GnRH agonists such as leuprolide require 2–3 weeks to achieve full suppression and are often associated with severe hypoestrogenic symptoms [16]. Progestins like dienogest remain effective but may induce irregular bleeding and weight gain with prolonged use [17]. Elagolix, by contrast, provides **rapid, reversible suppression** with favorable quality-of-life outcomes [18]. Furthermore, its oral route enhances compliance, especially in patients reluctant to undergo repeated injections or surgery.

Surgical management, while effective for immediate symptom relief, carries risk of adhesion formation and recurrence, with rates approaching 20–40% within 5 years [19]. In contrast, medical therapy such as elagolix may serve as a valuable **pre- or post-surgical adjunct**, minimizing recurrence by maintaining hormonal suppression [20]. Emerging combination strategies (elagolix with low-dose estrogen-progestin "add-back" therapy) have shown sustained efficacy over 12 months with minimal bone loss [21,22].

The present study's real-world design adds to existing clinical evidence, demonstrating that elagolix is both **clinically versatile and well-tolerated**, even in low-resource settings. However, limitations include relatively small sample size, single-center setting, and absence of long-term bone mineral density assessment. Larger multicenter studies are warranted to confirm its efficacy in rare subtypes such as umbilical or scar endometriosis and to explore optimized dosing schedules for different anatomical forms.

Overall, the study underscores that elagolix provides a **comprehensive, non-surgical treatment option** for diverse presentations of endometriosis—truly "beyond the ovary."

Limitations

- Observational design without a control group.
- Small number of extra-pelvic cases.
- Short-term follow-up (6 months).

Future controlled studies with larger samples and longer duration are recommended.

Conclusion

Elagolix represents a significant advancement in the medical management of endometriosis, offering an effective, rapid-onset, and reversible oral therapy that can be tailored to the individual's hormonal needs. In this study, elagolix not only alleviated chronic pelvic pain and dysmenorrhea in ovarian and deep infiltrating forms but also demonstrated promising symptom control in rare extra-pelvic sites such as umbilical and scar endometriosis.

The findings reinforce the concept that endometriosis is a systemic estrogen-dependent inflammatory disorder responsive to targeted hormonal modulation. With its favorable safety profile and high patient acceptability, elagolix provides a valuable non-surgical alternative or adjunct to traditional therapies.

Future multicenter studies with larger cohorts and longer follow-up are warranted to confirm its long-term benefits, explore add-back strategies, and evaluate its role in recurrence prevention. Overall, elagolix expands the therapeutic frontier of endometriosis treatment—**truly taking management beyond the ovary.**

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