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Assessment of Efficacy of Long Term (12 Months) Use of Dienogest in Women with Ovarian Endometriosis

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Abstract

Background: *Ovarian endometriosis is a chronic gynecological condition associated with pain, infertility and reduced quality of life. Dienogest, a selective progestin, has been proposed as an effective long-term medical therapy. This study aimed to evaluate the efficacy and safety of 12-month Dienogest therapy in women with ovarian endometriosis.*

Methods: *This prospective observational study was conducted at the Department of Obstetrics and Gynaecology, Bangladesh Medical University (BMU) from July 2024 to June 2025. A total of 240 women with diagnosed ovarian endometriosis were enrolled. Participants received 2 mg Dienogest daily for 12 months. Clinical assessment included endometrioma size (ultrasound), pain severity (VAS scores) and serum CA-125 levels at baseline, 3, 6, 9 and 12 months. Adverse events and treatment discontinuation were monitored. Data were analyzed using SPSS 25.*

Results: *The mean endometrioma diameter decreased from 46.7 ± 9.9 mm at baseline to 28.0 ± 6.9 mm at 12 months, a 40.0% reduction ($p<0.001$). Mean VAS scores declined from 7.9 ± 1.3 to 2.4 ± 1.2 and mean CA-125 levels reduced from 63.5 ± 25.7 U/mL to 33.4 ± 17.5 U/mL ($p<0.001$). The therapy was well tolerated; irregular uterine bleeding (20.4%) and weight gain >3 kg (14.6%) were the most common adverse events and only 13 participants (5.4%) discontinued treatment.*

Conclusion: *Long-term Dienogest therapy is effective in reducing endometrioma size, alleviating pain and lowering CA-125 levels, with good tolerability and low discontinuation rates. Continuous therapy offers a viable non-surgical option for managing ovarian endometriosis.*

Keywords: *Dienogest, ovarian endometriosis, endometrioma, pain, CA-125, long-term therapy.*

1. Introduction

Ovarian endometriosis, commonly referred to as endometrioma, is a frequent manifestation of endometriosis, characterized by the presence of ectopic endometrial tissue within the ovary [1]. It affects approximately 17–44% of women with endometriosis and is associated with chronic pelvic pain, dysmenorrhea, dyspareunia and infertility, significantly impairing quality of life [2]. The pathophysiology involves retrograde menstruation, hormonal imbalances, inflammation and local estrogen production, which together promote lesion growth and symptom persistence [3]. The chronic nature of the disease, coupled with a high recurrence rate after surgical excision, poses a therapeutic challenge for gynecologists, emphasizing the need for effective long-term medical management [4].

Hormonal therapy remains the mainstay of medical treatment for ovarian endometriomas, aiming to suppress ovulation, reduce lesion size, alleviate pain and prevent recurrence [5]. Dienogest, a fourth-generation selective

progestin with potent progestogenic activity and minimal androgenic effects, has demonstrated efficacy in inhibiting endometrial proliferation and inducing decidualization of ectopic endometrial tissue [6]. Unlike gonadotropin-releasing hormone (GnRH) analogues, Dienogest maintains a more favorable hormonal profile, with lower risks of hypoestrogenic side effects such as bone loss and vasomotor symptoms, making it suitable for long-term therapy [7].

Several studies have reported short- to medium-term benefits of Dienogest, including reduction in cyst size, improvement in pain scores and decreased serum CA-125 levels [8]. However, there is limited evidence on the sustained effectiveness of 12-month therapy in a larger cohort, particularly in South Asian populations, where epidemiological and clinical characteristics may differ. Furthermore, data on treatment adherence, safety profile and predictors of response remain scarce, underscoring the need for comprehensive prospective evaluations [9, 10].

Given its oral route, tolerability and potential for long-term use, Dienogest represents a promising alternative to repeated surgical interventions, which are associated with risks of ovarian reserve depletion and recurrence [11]. A thorough assessment of its long-term efficacy and safety is essential to inform clinical decision-making, optimize patient outcomes and provide evidence-based recommendations for the management of ovarian endometriomas [12].

The objective of this study was to evaluate the efficacy of 12-month Dienogest therapy in women with ovarian endometriosis by assessing changes in cyst size, pain severity, serum CA-125 levels and treatment-related adverse events.

2. Methodology & Materials

This prospective observational study was conducted at the Department of Obstetrics and Gynaecology, Bangladesh Medical University (BMU) from July 2024 to June 2025 and included 240 women diagnosed with ovarian endometriosis. Women aged 18–45 years with at least one ultrasound-confirmed ovarian endometrioma measuring ≥20 mm and experiencing symptoms such as dysmenorrhea, chronic pelvic pain, dyspareunia, or infertility, who were willing to undergo long-term medical therapy, were included. Patients were excluded if they were pregnant or breastfeeding, had known hypersensitivity to Dienogest, severe hepatic dysfunction, thromboembolic disorders, active psychiatric illness, prior use of gonadotropin-releasing hormone analogues or progestins within the last three months, or a desire to conceive during the treatment period. All participants received Dienogest 2 mg orally once daily for 12 months and adherence was monitored at each follow-up. Baseline evaluation included detailed history, clinical examination, transvaginal ultrasound for endometrioma size and laterality, serum CA-125 measurement and laboratory tests including complete blood count and liver function tests. Follow-up assessments were conducted at 3, 6, 9 and 12 months, recording pain severity using the visual analogue scale (VAS), cyst diameter via ultrasound, CA-125 levels at 6 and 12 months and adverse events. Rescue analgesics were permitted and documented. Data were entered and analyzed using SPSS version 25 and continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage. Paired t-tests were used to compare baseline and follow-up values of endometrioma diameter, VAS scores and CA-125 levels, whereas repeated measures analysis of variance (ANOVA) assessed changes over multiple time points. Chi-square or Fisher's exact tests were applied for categorical variables such as adverse events and treatment discontinuation. A p-value <0.05 was considered statistically significant.

3. Results

Table 1. *Baseline Characteristics of the Study Participants (n = 240)*

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	<25	27	11.3
	25–29	65	27.1
	30–34	71	29.6
	≥35	77	32
BMI (kg/m²)	Normal (18.5–24.9)	101	42.1
	Overweight (25–29.9)	95	39.6
	Obese (≥30)	44	18.3
Parity	Nulliparous	129	53.8

	Multiparous	111	46.2
Presenting Symptoms	Dysmenorrhea	213	88.8
	Chronic pelvic pain	157	65.4
	Dyspareunia	97	40.4
	Infertility	103	42.9
Laterality of Endometrioma	Unilateral	159	66.3
	Bilateral	81	33.7
Mean baseline cyst diameter	—	—	46.7 ± 9.9 mm

Table 1 shows the baseline characteristics of the 240 study participants. The majority were aged 30–34 years (29.6%) and had normal BMI (42.1%), while 53.8% were nulliparous. Most women reported dysmenorrhea (88.8%) and chronic pelvic pain (65.4%) and 66.3% had unilateral endometriomas. The mean baseline cyst diameter was 46.7 ± 9.9 mm.

Table 2. *Change in Endometrioma Size Over Time (n = 240)*

Time point	n	Mean ± SD diameter (mm)	Mean reduction (mm)	% Change	p-value
Baseline	240	46.7 ± 9.9	—	—	—
3 months	236	41.8 ± 9.1	4.9	−10.5 %	<0.001
6 months	231	37.5 ± 8.4	9.2	−19.7 %	<0.001
9 months	226	35.3 ± 7.8	11.4	−24.4 %	<0.001
12 months	219	28.0 ± 6.9	18.7	−40.0 %	<0.001

Table 2 illustrates the change in endometrioma size over the 12-month Dienogest treatment. The mean cyst diameter decreased from 46.7 ± 9.9 mm at baseline to 28.0 ± 6.9 mm at 12 months, representing a 40.0% reduction. Significant reductions were already observed at 3 months (41.8 ± 9.1 mm, −10.5%, p<0.001) and continued progressively through 6 and 9 months.

Table 3. *Pain (VAS) Scores and CA-125 Levels Over Time*

Time point	n (VAS)	Mean VAS ± SD	n (CA-125)	Mean CA-125 ± SD (U/mL)	p-value (vs baseline)
Baseline	240	7.9 ± 1.3	240	63.5 ± 25.7	—
3 months	238	5.8 ± 1.4	—	—	<0.001
6 months	232	4.2 ± 1.5	232	42.9 ± 20.6	<0.001
9 months	226	3.1 ± 1.3	—	—	<0.001
12 months	219	2.4 ± 1.2	219	33.4 ± 17.5	<0.001

Table 3 shows the changes in pain severity (VAS scores) and serum CA-125 levels during 12 months of Dienogest therapy. Mean VAS scores decreased from 7.9 ± 1.3 at baseline to 2.4 ± 1.2 at 12 months, while mean CA-125 declined from 63.5 ± 25.7 U/mL to 33.4 ± 17.5 U/mL. Significant improvements were observed as early as 3 months for pain (5.8 ± 1.4, p<0.001) and at 6 months for CA-125 (42.9 ± 20.6, p<0.001).

Table 4. *Adverse Events and Treatment Discontinuation (n = 240)*

Adverse Event	Frequency (n)	Percentage (%)	Severity
Irregular uterine bleeding	49	20.4	Mild–Moderate
Weight gain (>3 kg)	35	14.6	Mild
Headache	19	7.9	Mild
Breast tenderness	15	6.3	Mild
Mood changes	11	4.6	Mild–Moderate
Nausea	9	3.8	Mild
Decreased libido	7	2.9	Mild
Total discontinuations	13	5.4	—
• Due to adverse events	5	2.1	—
• Pregnancy during treatment	3	1.3	—
• Lost to follow-up	5	2.1	—

Table 4 summarizes adverse events and treatment discontinuation during 12 months of Dienogest therapy. The most common adverse events were irregular uterine bleeding (49, 20.4%) and weight gain >3 kg (35, 14.6%), mostly mild to moderate in severity. Overall, 13 participants (5.4%) discontinued treatment, including 5 due to adverse events (2.1%), 3 due to pregnancy (1.3%) and 5 lost to follow-up (2.1%).

4. Discussion

In this study, long-term (12 months) Dienogest therapy in women with ovarian endometriosis resulted in significant reductions in endometrioma size, pain severity and serum CA-125 levels, with a favorable safety profile. As observed in Table 2, the mean cyst diameter decreased by 40.0% from 46.7 ± 9.9 mm at baseline to 28.0 ± 6.9 mm at 12 months, which aligns with findings reported by Muzii et al., who demonstrated Dienogest's effectiveness in reducing disease and pain recurrence after endometriosis surgery [13].

Similarly, Wu et al. reported significant size reduction in deep infiltrating endometriosis with long-term Dienogest therapy [14]. These findings support the role of continuous progestin therapy in inhibiting ectopic endometrial proliferation and promoting regression of ovarian endometriomas, suggesting that long-term medical management may reduce the need for repeated surgical interventions, which are often associated with recurrence and potential compromise of ovarian reserve.

Pain relief was also notable, with mean VAS scores declining from 7.9 ± 1.3 to 2.4 ± 1.2 at 12 months (Table 3), consistent with prior studies. Maiorana et al. reported comparable improvement in pelvic pain after 12 months of Dienogest therapy, while Yu et al. showed sustained pain reduction over 28 weeks in women receiving Dienogest [15, 16].

The progressive decrease in pain scores in our cohort highlights Dienogest's efficacy in alleviating both chronic pelvic pain and dysmenorrhea, thereby improving overall quality of life. This effect may be attributed to its anti-proliferative and anti-inflammatory actions, which reduce ectopic endometrial activity and associated pelvic inflammation.

Serum CA-125 levels also decreased significantly from 63.5 ± 25.7 U/mL to 33.4 ± 17.5 U/mL, reflecting biochemical improvement alongside clinical outcomes. Andres et al. and Barra et al. similarly reported reductions in CA-125 and inflammatory markers with long-term Dienogest therapy, supporting the suppressive effect of Dienogest on ectopic endometrial tissue [17, 18]. Monitoring CA-125 provides an objective measure of therapeutic response and the marked reduction observed in our study emphasizes the efficacy of prolonged treatment.

The therapy was generally well tolerated, with irregular uterine bleeding (20.4%) and weight gain >3 kg (14.6%) being the most common adverse events (Table 4), while treatment discontinuation was low (5.4%). These safety outcomes are consistent with large prospective studies by Heinemann et al. and Cho et al., which reported mild to moderate adverse events and high adherence rates [19, 20]. Similarly, Caruso et al. and El Taha et al. demonstrated Dienogest's favorable tolerability compared to other hormonal regimens [21, 22]. Importantly, adverse events were predominantly mild and manageable, suggesting that long-term use is feasible in routine clinical practice without major safety concerns.

Overall, our findings reinforce the role of long-term Dienogest therapy as an effective and safe option for managing ovarian endometriomas, reducing cyst size, relieving pain and improving biochemical markers. The progressive improvement observed over 12 months highlights the benefit of continuous treatment, consistent with evidence from previous systematic reviews and meta-analyses [13, 15, 23]. These results provide valuable real-world evidence supporting the use of Dienogest as a first-line long-term medical therapy for endometriosis, particularly in women seeking symptom relief and fertility preservation, while avoiding repeated surgical interventions.

5. Limitations of the Study

This study was conducted at a single center, which may limit the generalizability of the findings. Additionally, follow-up beyond 12 months was not performed, so long-term recurrence rates and sustained safety could not be assessed. Some outcomes, such as pain scores, were self-reported and may be subject to subjective bias.

6. Conclusion

Long-term (12 months) Dienogest therapy is effective in reducing endometrioma size, alleviating pain and lowering CA-125 levels, with a favorable safety profile and low treatment discontinuation. Continuous use of Dienogest offers a non-surgical option for managing ovarian endometriosis, improving both clinical and biochemical outcomes while maintaining good tolerability.

7. Financial Support and Sponsorship

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8. CONFLICTS OF INTEREST

There are no conflicts of interest.

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