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## Original Research Article

# Efficacy of levonorgestrel releasing intrauterine system in the treatment of symptomatic adenomyosis: comparison with dienogest

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## ABSTRACT

**Background:** Adenomyosis is a common, estrogen-dependent, chronic gynecological condition that often presents with dysmenorrhea, menorrhagia, and an enlarged uterus. This study aimed to evaluate and compare the effectiveness of the levonorgestrel-releasing intrauterine system (LNG-IUS) and oral dienogest in the management of symptomatic adenomyosis.

**Methods:** This randomized controlled trial was conducted in the department of reproductive endocrinology and infertility, Bangabandhu Sheikh Mujib medical university (BSMMU), Dhaka, Bangladesh, from April 2022 to March 2023. In this study, we included 32 women aged 25-45 years diagnosed with symptomatic adenomyosis (menorrhagia and dysmenorrhea) attending the outpatient department of reproductive endocrinology and infertility at BSMMU. Participants were assigned to two treatment groups: One group received LNG-IUS and other group received dienogest.

**Results:** Baseline demographic and clinical characteristics were similar between the groups. The LNG-IUS group showed a significantly greater reduction in menstrual pain at both 3 months (VAS 1.7±2.9 vs. 4.1±2.8) and 6 months (VAS 0.9±2.5 vs. 3.9±3.0) compared to the dienogest group ( $p<0.05$ ). Uterine volume decreased more in the LNG-IUS group over time, but the differences were not statistically significant. Regular menstrual flow was significantly more common in the LNG-IUS group at both follow-ups, while heavy bleeding persisted in a notable portion of the dienogest group ( $p=0.004$  and  $p=0.002$ , respectively). Hemoglobin levels improved significantly more in the LNG-IUS group by 6 months (100% vs. 57.14%;  $p=0.017$ ). Although adverse effects were more frequently reported in the dienogest group, the difference was not statistically significant.

**Conclusions:** This study showed that LNG-IUS was more effective than oral dienogest in reducing pain, improving menstrual bleeding patterns, and increasing hemoglobin levels in women with symptomatic adenomyosis, with a lower incidence of side effects.

**Keywords:** Adenomyosis, LNG-IUS, Dienogest, Dysmenorrhea, Menorrhagia

## INTRODUCTION

Adenomyosis is a common, estrogen-dependent, benign gynecological condition. It is characterized by the presence of endometrial glands and stroma within the myometrium, forming either diffuse or localized lesions.<sup>1</sup> Approximately two-thirds of women diagnosed with adenomyosis experience symptoms, with menorrhagia and dysmenorrhea being the most prevalent. Other common findings include an enlarged, tender uterus and chronic pelvic pain.<sup>2</sup> Although adenomyosis typically affects women over the age of 40, it is also increasingly identified in younger women.<sup>3</sup> Reported prevalence of adenomyosis varies significantly, from 5% to 70%, depending on the diagnostic method used. However, its detection during hysterectomy is estimated at around 20-30%.<sup>4</sup>

Despite its prevalence, the exact pathogenesis and etiology of adenomyosis remain unclear. The most widely accepted theory suggests the invagination of the endometrial basal layer into the myometrium, possibly due to myometrial weakness or immune dysfunction, leading to a disruption of the endometrial-myometrial interface, also known as the junctional zone (JZ).<sup>5</sup>

Symptomatic adenomyosis is associated with increased uterine contractility and dysmenorrhea. Studies have shown elevated contractile amplitude and oxytocin receptor (OTR) expression in affected women, which correlates strongly with pain intensity.<sup>6,7</sup> Abnormal uterine contractions, along with increased nerve innervation, contribute to severe pelvic pain and play a central role in both disease progression and symptomatology.<sup>8</sup>

Adenomyosis has also been implicated in infertility. Proposed mechanisms include impaired sperm transport, abnormal uterine contractions, alterations in cell adhesion, dysregulated cell proliferation and apoptosis, and disruptions in free radical metabolism.<sup>5</sup> Furthermore, adenomyosis is recognized as a cause of recurrent implantation failure in women undergoing *in vitro* fertilization (IVF).<sup>9</sup>

Traditionally, adenomyosis was diagnosed through clinical evaluation and confirmed via histopathology after hysterectomy. However, non-invasive imaging modalities such as transvaginal ultrasonography (TVS) and magnetic resonance imaging (MRI) are now widely used and offer high diagnostic accuracy.<sup>10</sup> For women who do not desire fertility preservation, hysterectomy remains the only definitive treatment.<sup>5</sup> While less invasive options such as endometrial resection or ablation can improve menorrhagia, but they often fail to alleviate dysmenorrhea.<sup>11</sup> Medical management, typically modeled after endometriosis treatment, aims to reduce estrogen production or induce endometrial differentiation with progestins. The primary goals are to suppress ovulation, halt menstruation, and establish a stable hormonal environment, as both eutopic and ectopic endometria exhibit similar hormonal responses.

However, medical therapies are generally symptomatic rather than curative. Lesions tend to persist and become active again upon treatment cessation.<sup>12</sup> Hormonal options include oral contraceptives/low-dose estrogen-progestin combinations (OC/LEP), danazol, aromatase inhibitors (AI), and gonadotropin-releasing hormone analogs (GnRH-a), all of which are variably effective but associated with side effects and financial burdens.<sup>5</sup>

The LNG-IUS, initially approved in Europe in 1990 for contraception, has shown significant efficacy in managing menorrhagia and dysmenorrhea due to its localized endometrial suppression.<sup>2,12</sup> A systematic review and meta-analysis suggested that LNG-IUS is superior to other hormonal therapies for women seeking fertility preservation or avoiding hysterectomy, owing to its uterus-targeted action, minimal systemic hormone exposure, and long-acting, user-independent profile.<sup>14</sup> One randomized study involving 100 women with adenomyosis and heavy menstrual bleeding found that LNG-IUS reduced average blood loss by approximately 75%.<sup>15</sup>

Dienogest, a novel oral progestin derived from 19-nortestosterone, has high selectivity for progesterone receptors. Studies indicate it is highly effective in reducing adenomyosis-related pain.<sup>16</sup> Dienogest works by directly inhibiting cell proliferation and inducing apoptosis in adenomyotic cells.<sup>17</sup> It creates a mild hypoestrogenic and strong local hypergestagenic environment, leading to lesion atrophy without causing severe hypoestrogenic side effects. Given the hormonal similarities between adenomyosis and endometriosis, dienogest is considered a promising treatment alternative.<sup>18</sup> A retrospective cohort study also suggested dienogest is well-tolerated for long-term use until menopause, especially in patients with type 2 adenomyosis who wish to avoid surgery.<sup>16</sup>

A clinical trial by Ota et al demonstrated that both dienogest and LNG-IUS offer cost-effective, reversible, long-term treatment options for symptomatic adenomyosis, significantly reducing the need for surgical intervention.<sup>19</sup>

Therefore, the present study was designed to evaluate and compare the efficacy of LNG-IUS and dienogest in women suffering from symptomatic adenomyosis.

## METHODS

This randomized controlled trial was conducted in the department of reproductive endocrinology and infertility, BSMMU, Dhaka, Bangladesh, from April 2022 to March 2023. In this study, we included 32 women aged 25-45 years diagnosed with symptomatic adenomyosis (menorrhagia and dysmenorrhea) attending the outpatient department of reproductive endocrinology and infertility at BSMMU. Participants were assigned to two treatment groups: One group received LNG-IUS and the other group received dienogest.

These are the following criteria to be eligible for enrollment as our study participants:

### **Inclusion criteria**

Women aged between 25-45 years; diagnosed case of symptomatic adenomyosis (menorrhagia and dysmenorrhea) confirmed by transvaginal ultrasound; women not wishing to conceive for over 6 months; women with uterine size  $\leq 12$  gestational weeks were included.

### **Exclusion criteria**

Women with any contraindications with LNG-IUS or dienogest; women with ovarian endometrioma more than 3 cm in diameter; known case of cardiac, renal, or hepatic disease; women with undiagnosed vaginal bleeding; women with the presence of uterine fibroids, including submucosal fibroids; women with acute or chronic pelvic inflammation were excluded.

### **Intervention**

The study population comprised diagnosed cases of symptomatic adenomyosis. A total of 32 women were selected by purposive sampling according to the inclusion and exclusion criteria and were then divided into 2 groups.

**LNG-IUS group:** LNG-IUS (Eloira of Pregna International, India) was implanted into the uterine cavity during 5-7 days of the menstrual cycle in strict accordance with the operating instructions.

**Dienogest group:** Tablet dienogest 2 mg (tab. Dinogest of Nuvista Pharmaceuticals) orally once daily for 6 months. Treatment was started from days 2-5 of menstruation after the baseline visit.

### **Study procedure**

Women with symptomatic adenomyosis (presenting with dysmenorrhea and/or menorrhagia and confirmed by TVS) who met the inclusion and exclusion criteria were enrolled in the study. Baseline assessments included demographic data (age, occupation, residence, income), medical and surgical history, pain severity assessment using the visual analogue scale (VAS), menstrual pattern, uterine volume (via transvaginal ultrasound), and serum hemoglobin levels. Uterine volume was calculated using ellipsoid formula:  $0.52 \times \text{length} \times \text{anteroposterior} \times \text{transverse diameter}$ . Pain assessment was done using the 10 cm VAS, where 0 represented "no pain at all" and 10 denoted "worst imaginable pain." Participants marked their perceived pain intensity along this line, and the distance from the "no pain" end to the mark was recorded in centimeters as their pain score. Participants were counseled about the study's purpose, procedures, potential benefits, and side effects. Informed written consent was obtained before enrollment. Participants were contacted monthly by phone to monitor treatment adherence and identify any adverse effects.

Follow-up assessments were conducted at 3 months and 6 months, which included VAS pain scores, menstrual patterns (regular flow, heavy flow, spotting, or amenorrhea), uterine volume, hemoglobin levels, and documentation of any adverse events.

### **Data collection and analysis**

Data were collected through interviews, history sheets, physical and lab examinations using a structured questionnaire containing all variables of interest. All data were recorded systematically in a pre-formatted data collection form. Quantitative data was expressed as mean and standard deviation, and qualitative data was expressed as frequency distribution and percentage. Chi-square and Fisher's exact test analyzed categorical variables, shown with cross tabulation. Student t test and paired t test were used for continuous variables.  $P < 0.05$  was considered significant. Statistical analysis was performed using SPSS 26 (Statistical package for social sciences) for Windows version 10. This study ethically approved by institutional review board of BSMMU, Dhaka, Bangladesh.

## **RESULTS**

This randomized controlled trial included a total of 32 patients diagnosed with symptomatic adenomyosis, confirmed by transvaginal ultrasound, who were enrolled and randomly assigned to two treatment groups using sequentially numbered, sealed opaque envelopes. In the LNG-IUS group, 16 patients received the LNG-IUS, while in the dienogest group, 16 patients were prescribed oral dienogest (2 mg once daily). One patient in the LNG-IUS group dropped out after three months due to the spontaneous expulsion of the device. In the dienogest group, two patients discontinued treatment—one was lost to follow-up, and the other stopped medication after three months due to irregular vaginal bleeding. Data from the remaining participants in both groups were analyzed. The results are presented in the following tables.

Table 1 shows that the mean age of participants was slightly higher in the LNG-IUS group ( $34.8 \pm 4.7$  years) compared to the dienogest group ( $32.0 \pm 5.3$  years), though this difference was not statistically significant ( $p = 0.134$ ). Occupational and educational status distributions were similar between the groups, with the majority of participants being housewives and having education levels of HSC or above. No statistically significant differences were observed in occupational status ( $p = 0.255$ ) or educational status ( $p = 0.677$ ). The mean BMI was comparable between the two groups ( $27.8 \pm 2.8$  in LNG-IUS vs.  $27.7 \pm 3.5$  in dienogest;  $p = 0.932$ ). Regarding parity, the majority of participants were multiparous in both groups, with no significant difference observed ( $p = 0.446$ ).

Table 2 shows that at pretreatment, the VAS score was not statistically significant between the two groups. After 3 months of treatment, mean VAS score was significantly decreased in the LNG-IUS group than the dienogest group

(1.7±2.9 vs 4.1±2.8) with 95% CI -4.47 to -0.28%. After 6 months of treatment, mean VAS score was significantly

decreased in the LNG-IUS group than the dienogest group (0.9±2.5 vs 3.9±3.0) with a 95% CI of -5.01 to -0.83%.

**Table 1: Socio-demographic characteristics of the study subjects, (n=32).**

| Demographic characteristics   | LNG-IUS group, (n=16) (%) |          | Dienogest group, (n=16) (%) |          | P value                          |
|-------------------------------|---------------------------|----------|-----------------------------|----------|----------------------------------|
|                               | Mean                      | ±SD      | Mean                        | ±SD      |                                  |
| <b>Age (in years)</b>         | 34.8                      | ±4.7     | 32.0                        | ±5.3     | <sup>a</sup> 0.134 <sup>ns</sup> |
| Range (min-max)               | 28.0                      | -43.0    | 25.0                        | -42.0    |                                  |
| <b>Occupational status</b>    |                           |          |                             |          | <sup>b</sup> 0.255 <sup>ns</sup> |
| Housewife                     | 11                        | 68.75    | 11                          | 68.75    |                                  |
| Service holder                | 2                         | 12.50    | 0                           | 0.00     |                                  |
| Teacher                       | 2                         | 12.50    | 1                           | 6.25     |                                  |
| Student                       | 0                         | 0.00     | 3                           | 18.75    |                                  |
| Garments worker               | 1                         | 6.25     | 1                           | 6.25     |                                  |
| <b>Educational status</b>     |                           |          |                             |          | <sup>b</sup> 0.677 <sup>ns</sup> |
| Illiterate                    | 1                         | 6.25     | 0                           | 0.00     |                                  |
| Primary                       | 1                         | 6.25     | 2                           | 12.50    |                                  |
| SSC                           | 3                         | 18.75    | 4                           | 25.00    |                                  |
| HSC or above                  | 11                        | 68.75    | 10                          | 62.50    |                                  |
| <b>Residence</b>              |                           |          |                             |          | <sup>b</sup> 1.00 <sup>ns</sup>  |
| Rural                         | 9                         | 56.25    | 9                           | 56.25    |                                  |
| Urban                         | 7                         | 43.75    | 7                           | 43.75    |                                  |
| <b>BMI (kg/m<sup>2</sup>)</b> |                           |          |                             |          | <sup>a</sup> 0.932 <sup>ns</sup> |
| 18.5-24.9                     | 2                         | 12.50    | 4                           | 25.00    |                                  |
| 25.0-29.9                     | 12                        | 75.00    | 8                           | 50.00    |                                  |
| ≥30.0                         | 2                         | 12.50    | 4                           | 25.00    |                                  |
| Mean±SD                       | 27.8                      | ±2.8     | 27.7                        | ±3.5     |                                  |
| Range (min-max)               | 23.0                      | -34.2    | 22.0                        | -36.7    |                                  |
| <b>Monthly income (Taka)</b>  | 32937.5                   | ±22643.5 | 27968.8                     | ±11875.0 | <sup>a</sup> 0.443 <sup>ns</sup> |
| Range (min-max)               | 10000                     | -100000  | 12500                       | -50000   |                                  |
| <b>Parity</b>                 |                           |          |                             |          | <sup>b</sup> 0.446 <sup>ns</sup> |
| Nullipara                     | 4                         | 25.00    | 6                           | 37.50    |                                  |
| Multipara                     | 12                        | 75.00    | 10                          | 62.50    |                                  |

\*ns=not significant, <sup>a</sup>p value reached from unpaired t-test, <sup>b</sup>p value reached from chi-square test.

**Table 2: Pretreatment and post-treatment comparison of VAS score between LNG-IUS group and dienogest group.**

| VAS score                          | LNG-IUS group, n=15 |      | Dienogest group, n=14 |      | 95% CI         | P value             |
|------------------------------------|---------------------|------|-----------------------|------|----------------|---------------------|
|                                    | Mean                | ±SD  | Mean                  | ±SD  |                |                     |
| <b>Pretreatment</b>                | 9.4                 | ±0.7 | 9.0                   | ±0.9 | -0.15 to 1.02  | 0.140 <sup>ns</sup> |
| <b>After 3 months of treatment</b> | 1.7                 | ±2.9 | 4.1                   | ±2.8 | -4.47 to -0.28 | 0.028 <sup>s</sup>  |
| <b>After 6 months of treatment</b> | 0.9                 | ±2.5 | 3.9                   | ±3.0 | -5.01 to -0.83 | 0.008 <sup>s</sup>  |

\*1 case dropout from the LNG-IUS group; 2 cases dropped out after 3 months in the dienogest group, s=significant; ns=not significant

**Table 3: Pre and post-treatment comparison of uterine volume between LNG-IUS group and dienogest group.**

| Uterine volume (ml)                 | LNG-IUS group |        | Dienogest group |        | 95% CI           | P value             |
|-------------------------------------|---------------|--------|-----------------|--------|------------------|---------------------|
|                                     | Mean          | ±SD    | Mean            | ±SD    |                  |                     |
| <b>Pretreatment</b>                 | 196.0         | ±109.7 | 191.7           | ±101.7 | -72.12 to 80.70  | 0.910 <sup>ns</sup> |
| <b>After 3 months of treatment*</b> | 167.2         | ±105.9 | 189.8           | ±104.6 | -99.98 to 54.76  | 0.555 <sup>ns</sup> |
| <b>After 6 months of treatment</b>  | 146.9         | ±109.2 | 192.1           | ±106.1 | -127.26 to 36.99 | 0.269 <sup>ns</sup> |

\*1 case dropout from the LNG-IUS group; 2 cases dropped out after 3 months in the Dienogest group, s=significant; ns=not significant

Table 3 shows that before treatment; there was no significant difference in mean uterine volume between the LNG-IUS group (196.0±109.7 ml) and the dienogest group (191.7±101.7 ml; p=0.910). After 3 months of treatment, a slight reduction in uterine volume was

observed in the LNG-IUS group (167.2±105.9 ml), while the dienogest group showed minimal change (189.8±104.6 ml). However, the difference between the groups was not statistically significant (p=0.555; 95% CI: -99.98 to 54.76). At 6 months, a further decrease in

uterine volume was noted in the LNG-IUS group ( $146.9 \pm 109.2$  ml), whereas dienogest group remained relatively unchanged ( $192.1 \pm 106.1$  ml). Despite this, the difference between the two groups remained statistically non-significant ( $p=0.269$ ; 95% CI: -127.26 to 36.99).

Table 4 shows that at pretreatment, the majority of patients had heavy bleeding in both groups, which was not significant. After 3 months of treatment, in the LNG-IUS group, 14 (87.50%) patients had regular flow, whereas 5 (33.33%) patients of the dienogest group had heavy bleeding; the difference was significant ( $p=0.004$ ). After 6 months of treatment, spotting was found in 1 (6.67%) patient in the LNG-IUS group and 2 (14.29%) in the dienogest group. Spotting+ regular was found in 1 (6.67%) patient of the LNG-IUS group. Regular flow was higher in the LNG-IUS group (86.67%), but heavy bleeding persisted among 6 (42.86%) patients of dienogest group, which was higher (42.86%) compared to the LNG-IUS group, which was significant between 2 groups ( $p=0.002$ ).

Table 5 shows that after 6 months of treatment, all patients (100%) in the LNG-IUS group experienced an increase in hemoglobin levels, compared to 57.14% of patients in the dienogest group. This difference was statistically significant ( $p=0.017$ ). However, at the 3-month follow-up, hemoglobin levels had increased in 75% of patients in the LNG-IUS group and 40% in dienogest group, though this difference did not reach statistical significance ( $p=0.124$ ).

Table 6 highlights the adverse effects reported in both groups. In the LNG-IUS group, 2 patients (12.5%) reported abnormal uterine bleeding, while 1 patient each (6.3%) experienced weight gain and intrauterine device displacement. In contrast, the dienogest group showed a higher frequency of side effects: 6 patients (40.0%) reported abnormal uterine bleeding, and 2 patients each (13.3%) experienced headache, weight gain, or breast tenderness. One patient (6.7%) also reported nausea. Despite the higher number of adverse events in the dienogest group, the differences between the two groups were not statistically significant ( $p>0.05$ ).

**Table 4: Pret and post-treatment comparison of pattern of menstrual flow between LNG-IUS and dienogest group.**

| Pattern of menstrual flow          | LNG-IUS group  |       | Dienogest group |       | P value             |
|------------------------------------|----------------|-------|-----------------|-------|---------------------|
|                                    | N              | %     | N               | %     |                     |
| <b>Pretreatment</b>                | <b>(n=16)</b>  |       | <b>(n=16)</b>   |       |                     |
| Regular flow                       | 3              | 18.75 | 3               | 18.75 | 0.673 <sup>ns</sup> |
| Heavy flow                         | 13             | 81.25 | 13              | 81.25 |                     |
| <b>After 3 months of treatment</b> | <b>(n=16)</b>  |       | <b>(n=15)*</b>  |       |                     |
| Spotting                           | 0              | 0.00  | 2               | 13.33 | 0.004 <sup>s</sup>  |
| Regular flow                       | 14             | 87.50 | 4               | 26.67 |                     |
| Heavy flow                         | 0              | 0.00  | 5               | 33.33 |                     |
| Amenorrhea                         | 2              | 12.50 | 4               | 26.67 |                     |
| <b>After 6 months of treatment</b> | <b>(n=15)*</b> |       | <b>(n=14)*</b>  |       |                     |
| Spotting                           | 1              | 6.67  | 2               | 14.29 | 0.002 <sup>s</sup>  |
| Spotting +regular                  | 1              | 6.67  | 0               | 0.00  |                     |
| Regular flow                       | 13             | 86.67 | 3               | 21.43 |                     |
| Heavy flow                         | 0              | 0.00  | 6               | 42.86 |                     |
| Amenorrhea                         | 0              | 0.00  | 3               | 21.43 |                     |

\*1 case dropout from the LNG-IUS group; 2 cases dropped out after 3 months in the dienogest group, s=significant; ns=not significant.

**Table 5: Pretreatment and post-treatment comparison of Hb level between LNG-IUS group and dienogest group.**

| Hemoglobin (gm/dl)                 | LNG-IUS group  |        | Dienogest group |       | P value             |
|------------------------------------|----------------|--------|-----------------|-------|---------------------|
|                                    | N              | %      | N               | %     |                     |
| <b>After 3 months of treatment</b> | <b>(n=16)</b>  |        | <b>(n=15)*</b>  |       |                     |
| Increased                          | 12             | 75.00  | 6               | 40.00 | 0.124 <sup>ns</sup> |
| Decreased                          | 2              | 12.50  | 6               | 40.00 |                     |
| No change                          | 2              | 12.50  | 3               | 20.00 |                     |
| <b>After 6 months of treatment</b> | <b>(n=15)*</b> |        | <b>(n=14)*</b>  |       |                     |
| Increased                          | 15             | 100.00 | 8               | 57.14 | 0.017 <sup>s</sup>  |
| Decreased                          | 0              | 0.00   | 5               | 35.71 |                     |
| No change                          | 0              | 0.00   | 1               | 7.14  |                     |

\*1 case dropped out from LNG-IUS group; 2 dropped out before and after 3 months in dienogest group, s=significant, ns=not significant.



**Table 6: Distribution of the study patients by side effect.**

| Side effects                     | LNG-IUS group, (n=16) |      | Dienogest group, (n=15*) |      | P value             |
|----------------------------------|-----------------------|------|--------------------------|------|---------------------|
|                                  | N                     | %    | N                        | %    |                     |
| Headache                         | 0                     | 0.0  | 2                        | 13.3 | 0.226 <sup>ns</sup> |
| Weight gain                      | 1                     | 6.3  | 2                        | 13.3 | 0.600 <sup>ns</sup> |
| Nausea                           | 0                     | 0.0  | 1                        | 6.7  | 0.484 <sup>ns</sup> |
| Breast tenderness                | 0                     | 0.0  | 2                        | 13.3 | 0.226 <sup>ns</sup> |
| Abnormal uterine bleeding        | 2                     | 12.5 | 6                        | 40.0 | 0.113 <sup>ns</sup> |
| Intrauterine device displacement | 1                     | 6.3  | 0                        | 0.0  | 1.000 <sup>ns</sup> |

\*1 case dropout due to discontinuation of treatment before 3 months in the dienogest group, ns=not significant.

## DISCUSSION

In the present study, the mean age was  $34.8 \pm 4.7$  years in the LNG-IUS group and  $32.0 \pm 5.3$  years in the dienogest group, with no statistically significant difference ( $p=0.134$ ). This finding aligns with that of Xu et al who reported mean ages of 36.9 years in the LNG-IUS group and 36.7 years in the dienogest group ( $p=0.38$ ).<sup>20</sup> Similarly, Yang et al reported a mean age of  $40.86 \pm 5.56$  years in the LNG-IUS group and  $41.44 \pm 5.28$  years in the dienogest group, with no significant difference ( $p>0.05$ ), though the participants in their study were older.<sup>21</sup>

Regarding BMI, the present study found a mean BMI of  $27.8 \pm 2.8$  kg/m<sup>2</sup> in the LNG-IUS group and  $27.7 \pm 3.5$  kg/m<sup>2</sup> in the dienogest group, with no significant difference ( $p=0.832$ ). Xu et al reported lower average BMIs of 22.1 kg/m<sup>2</sup> and 22.7 kg/m<sup>2</sup>, respectively ( $p=0.34$ ).<sup>20</sup> Lee et al found mean BMIs of  $22.1 \pm 3.2$  kg/m<sup>2</sup> in the LNG-IUS group and  $20.8 \pm 0.2$  kg/m<sup>2</sup> in the dienogest group while Park et al and Neriishi et al also reported lower BMI values.<sup>10,16,22</sup> The higher BMI in our study population may be due to a higher prevalence of overweight and obesity among participants.

For dysmenorrhea assessment using the VAS, pretreatment scores were similar between groups ( $9.4 \pm 0.7$  in LNG-IUS vs.  $9.0 \pm 0.9$  in dienogest;  $p>0.05$ ). At 3 months, VAS scores significantly improved in the LNG-IUS group ( $1.7 \pm 2.9$ ) compared to the dienogest group ( $4.1 \pm 2.8$ ), with a 95% CI of -4.47 to -0.28. At 6 months, the trend continued ( $0.9 \pm 2.5$  vs.  $3.9 \pm 3.0$ ; 95% CI: -5.01 to -0.83). Interestingly, Yang et al found dienogest to be more effective in reducing VAS scores over 3, 6, and 12 months.<sup>21</sup> Lee et al reported lower mean VAS scores in the LNG-IUS group after 6 months ( $1.0 \pm 1.0$  vs.  $1.4 \pm 2.2$ ;  $p<0.05$ ).<sup>22</sup> Ota et al observed both treatments to be effective in reducing pain, although dienogest showed quicker results at 3 months.<sup>19</sup>

In the present study, at baseline, the uterine volumes were similar between groups ( $196.0 \pm 109.7$  ml in LNG-IUS vs.  $191.7 \pm 101.7$  ml in dienogest;  $p=0.910$ ). After 6 months, there was a greater reduction in uterine volume in the LNG-IUS group ( $146.9 \pm 109.2$  ml) compared to the dienogest group ( $192.1 \pm 106.1$  ml), though the difference

between groups was not statistically significant ( $p=0.269$ ). However, the reduction within the LNG-IUS group was significant compared to baseline ( $p=0.001$ ), while no significant change was observed in the dienogest group. Xu et al reported similar findings, with no improvement in uterine volume after dienogest treatment, and only a slight, non-significant reduction in the LNG-IUS group.<sup>20</sup>

Yang et al however, found significantly greater reductions in uterine volume in the LNG-IUS group at 12 months ( $p<0.001$ ).<sup>21</sup>

In terms of menstrual bleeding, most participants initially presented with heavy bleeding. After 3 months, 87.5% of the LNG-IUS group reported regular flow, while 33.3% of the dienogest group continued to experience heavy bleeding ( $p=0.004$ ). At 6 months, 86.67% of LNG-IUS users had regular flow, while 42.86% of dienogest users still experienced heavy bleeding, and this finding was statistically significant ( $p=0.002$ ). Yang et al observed a more pronounced long-term benefit of dienogest in reducing menstrual volume.<sup>21</sup> Ota et al also noted that irregular bleeding was more frequent with LNG-IUS, especially in the early months, although this decreased over time with dienogest.<sup>19</sup>

In our study, hemoglobin levels improved in both groups. At 3 months, 75% of patients in the LNG-IUS group showed improvement versus 40% in the dienogest group ( $p=0.124$ ). At 6 months, all patients in the LNG-IUS group had increased hemoglobin levels compared to 57.14% in the dienogest group, which was statistically significant ( $p=0.017$ ). Xu et al similarly reported a significant increase in hemoglobin in the LNG-IUS group, but only a marginal, non-significant improvement in the dienogest group.<sup>20</sup>

Regarding adverse effects, the LNG-IUS group had fewer reported events: 2 patients (12.5%) reported abnormal bleeding, and one patient each (6.3%) experienced weight gain or device displacement. In the dienogest group, 6 patients (40%) had abnormal bleeding, and 2 patients each (13.3%) experienced headache, weight gain, or breast tenderness; 1 patient (6.7%) reported nausea. Although adverse effects were more frequent in the dienogest group,

the difference was not statistically significant ( $p>0.05$ ). Xu et al reported higher rates of abnormal uterine bleeding and other side effects in the dienogest group.<sup>20</sup> Ota et al noted that irregular bleeding was a common issue with dienogest but could be mitigated with continuous use.<sup>19</sup> A previous study by Park et al also found that irregular bleeding was a frequent side effect in patients treated with dienogest for endometriosis.<sup>23</sup>

### Limitations

Our study was a single-center study, and the study period was short. We took a small sample size, so it does not represent the whole community. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

### CONCLUSION

In our study, we found that both LNG-IUS and dienogest are effective in managing symptoms such as dysmenorrhea and menorrhagia associated with adenomyosis. However, LNG-IUS demonstrated superior outcomes in reducing pain, improving menstrual bleeding patterns, and increasing hemoglobin levels, with fewer reported adverse effects. This study suggests that LNG-IUS is more effective than oral dienogest as a more favorable therapeutic option for long-term symptom control in women with adenomyosis.

Further study with a prospective and longitudinal study design, including a larger sample size with long-term follow-up, needs to be done to establish the long-term efficacy and safety of LNG-IUS and dienogest.

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