Table 1
Characteristics of vaginal samples from Portuguese women (n = 260).[a]

Characteristic	*Gardnerella vaginalis* positive (n = 96)	*Gardnerella vaginalis* negative (n = 164)
Age, y	33 ± 11	31 ± 12
Previously diagnosed with bacterial vaginosis	23 (24.0)	29 (17.7)
Diagnosed with bacterial vaginosis more than once	10 (10.4)	13 (7.9)
Current symptoms		
Itching	13 (13.5)	11 (6.7)
Pain	4 (4.2)	8 (4.9)
Increased vaginal discharge	9 (9.4)	17 (10.4)
Odor	13 (13.5)	9 (5.5)
Burning	12 (12.5)	11 (6.7)
Smoker	15 (15.6)	26 (15.9)
Chronic disease	23 (24.0)	33 (20.1)
Tampon user	41 (42.7)	82 (50.0)
Contraception		
No answer	0 (0.0)	4 (2.4)
No contraception	16 (16.7)	30 (18.3)
Pill	62 (64.6)	92 (56.1)
Condom	15 (15.6)	43 (26.2)
Other	13 (13.5)	25 (15.2)
Change in sexual partner in the past 3 months	2 (2.1)	9 (5.5)
Children	34 (35.4)	52 (31.7)
Premature children	2 (2.1)	3 (1.8)
Presence of *Atopobium vaginae*[b]	23 (24.0)	7 (4.3)

[a] Values are given as mean ± SD or number (percentage).
[b] Factor associated with significant difference between groups ($P < 0.05$).

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The effect of levonorgestrel intrauterine device placement on serum CA-125 levels in healthy premenopausal women

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Cancer antigen 125 (CA-125) is a glycoprotein found on the surface of cells originating from embryonic coelomic epithelium, including epithelium of the fallopian tubes, endometrium, and endocervix [1]. Many causes of abdominopelvic inflammation have been associated with elevations in CA-125 levels, including pelvic inflammatory disease of which endometritis is a component [2]. Levonorgestrel intrauterine devices (IUDs) have been associated with endometrial stromal leukocytic infiltrates, focal necrosis, and scarring [3]. The present study was conducted to determine the effect of levonorgestrel IUD placement on CA-125 levels in healthy women of reproductive age.

Healthy premenopausal women aged 18–50 years seeking a levonorgestrel IUD (Mirena; Bayer HealthCare, Wayne, NJ, USA) for contraception at a single academic hospital in Ann Arbor, MI, USA, between January 10, 2011, and January 9, 2012, were recruited. Exclusion criteria included suspected endometriosis, known endometriosis or adenomyosis, irregular menstrual periods, history of malignancy, any inflammatory process of the pleura or peritoneum, pregnancy within the previous 12 weeks, IUD placement within the previous 12 weeks, or known adnexal mass. Women who were unable to undergo pre-insertion blood draw at least 3 days remote from recent or expected menses were also excluded. The study was approved by the institutional review board at the University of Michigan. All participants provided written informed consent.

Prior to IUD insertion, a blood sample was taken; a repeat sample was drawn 12 weeks after placement. Vaginal bleeding around the second blood draw was recorded. Compensation (US $10) was provided per completed blood draw. Blood samples were analyzed using the ADVIA CA 125II chemiluminescent immunoassay (Siemens Healthcare Diagnostics, Deerfield, IL, USA). Demographics were collected from hospital records.

Power calculations revealed that 13 patients would be required to show a difference in CA-125 of 5 U/mL using a 2-tailed test, assuming a baseline CA-125 level of 10 U/mL at 90% power. Data were analyzed using SPSS version 20 (IBM, Armonk, NY, USA); paired *t* test and Pearson correlation were used for analysis as appropriate. Statistical significance was determined at the 0.05 level.

Sixteen women were recruited, all of whom completed the pre-insertion blood draw. The mean age of the participants was 30 ± 8 years (range, 19–50 years). Body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) ranged from 17.5 to 38.6, with mean of 23.9 ± 5.8. Mean gravidity was 2.0 ± 2.5 and mean parity was 1.9 ± 2.8. The majority of the women identified as white (n = 13), while 2 identified as South Asian and 1 as Hispanic. None of the participants reported current tobacco use. Intrauterine device placement was ceased in 1 patient

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owing to cervical stenosis, and 2 women were lost to follow-up; the remaining 13 participants completed the study.

Mean pre-insertion CA-125 was 10.7 ± 5.9 U/mL (range, 3.3–22 U/mL), while mean post-placement CA-125 was 8.5 ± 4.2 U/mL (range, 2.8–18.5 U/mL) (Table 1); no significant difference was found between these values ($P = 0.124$). Moderate or severe dysmenorrhea was present in 6 women; it was not associated with higher pre-insertion CA-125 (11.3 vs 10.0 U/mL; $P = 0.675$). Bleeding within 3 days of the post-placement blood draw was documented in 4 participants; it was significantly associated with higher post-placement CA-125 (12.3 vs 6.8 U/mL; $P = 0.022$). Mean time from levonorgestrel IUD placement to post-placement blood draw was 14.7 ± 2.8 weeks (range, 12.1–22.4 weeks). No correlation was found between any measure of CA-125 and age, BMI, gravidity, or parity.

Given the focal endometrial inflammation and necrosis seen with levonorgestrel IUDs throughout the time that they remain in situ [3], we would have expected a small increase in serum CA-125 when controlling for other known variables. However, the study failed to show such a finding. Instead, average pre- and post-IUD placement CA-125 levels were statistically similar. This indicates that a simple mechanism for CA-125 release into serum as a result of necrosis or inflammation of the endometrium does not account for the observed physiology in this population. Using ±3 days to control for bleeding at the time of the post-placement blood draw was arbitrarily determined but it did demonstrate utility in differentiating the effect of vaginal bleeding on serum CA-125. The only other study to have examined serum CA-125 levels in healthy women with IUD placement involved the copper IUD [4]. The findings from that study demonstrated a significant decrease in CA-125 after placement [4]. However, both pre- and post-placement CA-125 levels were measured during menstruation, and the average pre-insertion CA-125 level was higher than reported in other studies.

In the present study, consistent with results from other investigations [4], CA-125 levels in healthy women did not significantly increase with IUD placement, despite being elevated in women with pelvic inflammatory disease. Based on these results, it appears that isolated coelomic epithelial inflammation of endometrial origin as caused by IUDs does not result in an elevation of serum CA-125 in otherwise healthy women.

Table 1
Serum CA-125.

CA-125 measurement	Mean ± SD (range)
Pre-insertion, U/mL (n = 16)	10.7 ± 5.9 (3.3–22)
Post-placement, U/mL (n = 13)	8.5 ± 4.2 (2.8–18.5)
Difference, U/mL[a] (n = 13)	−2.2 ± 4.8 (−12 to 3.9)

Abbreviation: CA-125, cancer antigen 125.
[a] Pre-insertion CA-125 subtracted from post-placement CA-125.

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Conflict of interest

The authors have no conflicts of interest.

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