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Comparison of copper IUDs and hormonal IUDs in prevalence of *Candida* species in cervicovaginal smears

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ABSTRACT

Candidal vulvovaginitis is one of the most common genital infections that different types of diagnosis are essential for a proper treatment plan. IUD is one of the most influential and long-lasting methods of contraception that can be associated with vaginal candidiasis. This study was performed to investigate the prevalence of Candida species before and three months after IUD placement in patients referred to health centers. Also, a comparison of copper IUDs and hormonal IUDs was evaluated to consider the prevalence of Candida species in cervicovaginal smears. In this regard, cervicovaginal swabs were prepared from 160 women applying for IUDs who did not show signs of vaginal infection during the vaginal examination. These people were divided into two groups of 80 cases. The first group received copper IUDs (NT Cu380, Mona Lisa®, Canada), and the second group received hormonal IUDs (Mirena, USA). They had not used antibiotics or antifungal drugs at least two weeks before and three months after IUD placement. The provided Samples were cultured in a Saburo dextrose agar medium. The milky yeast colony was transferred to chromium agar culture medium, and fungal species were differentiated by dyeing. P <0.05 was considered significant. Three months after IUD insertion, 29.57% of people who received a copper IUD were diagnosed with candidiasis. Also, different species of Candida were observed in 22.95% of people who received hormonal IUD. Because *Candida albicans* is found in the vaginal microflora of 30 to 80% of asymptomatic women, the decision to treat asymptomatic cases requires further study and testing. The use of Candida chromium agar differential culture medium is easy, reproducible, and cost-effective; however, in cases such as recurrent or complicated vulvovaginal candidiasis where the accurate diagnosis is essential for successful treatment, the use of sensitive and precise molecular methods such as PCR is recommended. Finally, studies with wider dimensions and longer follow-up periods are suggested to confirm and complete the present study.

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Introduction

The intrauterine device (IUD) is recognized as one of the important choices in long-term contraception (about five years) (1). An IUD is a T-shaped implant made of metal or polymer inserted into the uterine cavity and plays a role in the gradual release of hormones or copper ions (2). In general, two types of IUDs are used. The first group releases contraceptive hormones such as levonorgestrel (LNg) (3). The second group is hormone-free IUDs, which gradually release copper ions, also known as copper IUDs (4). The most critical weakness of copper IUDs is the high risk of bleeding and pain due to their placement, which is mainly related to the speed of copper release (5). It is reported that more than 67% of women who used Cu T380 (a type of copper-based IUD) complained of menstrual side effects in the first year of use. The rate of IUD degradation is noticeably high in the early days after placement, also known as the explosive release of copper ions (5). PLGA (with a ratio of 75/25 of lactic acid/glycolic acid) is considered one of the polymers in IUD development by its biodegradability, biocompatibility, and mechanical properties (6).

In IUDs, the altered environment of the uterus interferes with the passage of sperm through the uterus and prevents fertility. All IUDs stimulate the formation of prostaglandins in the uterus, which cause smooth muscle contraction and inflammation (7). Prostaglandins also reduce the local cellular immune response (8). The IUD body also facilitates the binding, colonization, and biofilm formation by

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Candida species. Biofilm formation is also associated with acute and chronic candidiasis (9). In a study by Levin et al. (10), they found that the risk of pelvic inflammatory disease (PID) increased in the first 20 days after IUD placement. Several studies have shown an increased incidence of candidiasis with IUD placement. For example, Guzel et al. (11) showed that IUD was associated with an increased risk of acute and recurrent candidiasis. However, some studies did not find a significant relationship in this regard. For example, Demirezen et al. (12) did not find a significant association between IUD placement and candidiasis. However, they showed that patients with prolonged IUD use were more likely to have a fungal infection.

Infection can be minimized through careful screening and the use of aseptic techniques. These methods include sugar absorption kits and culture in differential media such as chromium agar (13, 14). The chromium agar method distinguishes the five most common species of Candida by dyeing (14). In many studies, chromium agar culture medium has been used as an easy and reliable method to identify several isolated species of patients with vulvovaginal candidiasis (15). This study used this method to identify and compare Candida species before and three months after IUD placement. Also, a comparison of copper IUDs and hormonal IUDs was evaluated to consider the prevalence of Candida species in cervicovaginal smears.

Materials and methods

This prospective longitudinal study was performed on 160 women who volunteered for IUD use and were referred to health centers. People were similar in terms of social, economic, and living conditions. These people were divided into two groups of 80 cases. The first group received copper IUDs (NT Cu380, Mona Lisa®, Canada), and the second group received hormonal IUDs (Mirena, USA). Sampling and completing the questionnaire were done with the full consent of the individuals. After providing full explanations about the study by the researcher, a written consent form was obtained from them. No case of clinical candidiasis was seen before IUD placement. Three months after the IUD was inserted, people with symptomatic infections were given medical advice and treatment.

Inclusion criteria included: no absolute and relative contraindications to IUD placement, including clinical cervicitis and clinical vaginitis, no history of antibiotics, and systemic or vaginal antifungal drugs from two weeks before IUD placement. In addition, none of the cases had diabetes, Wilson's disease, immune deficiency, severe anemia, and coagulation disorders.

Exclusion criteria included IUD withdrawal for any reason within three months after placement and use of systemic or topical drugs affecting the cervicovaginal fungal flora within two weeks before the second sampling (three months after IUD placement).

At the beginning of the study, the researcher completed a questionnaire including demographic information and midwifery records for all participants.

Before IUD insertion with speculum insertion, the cervicovaginal specimen was prepared by sterile swab from the posterior fornix of the vagina and transferred to a laboratory in a Falcon containing 1.5 ml of sterile buffer (PBS). The samples were cultured on Saboro dextrose agar (SDA) medium and then placed in a 37°C incubator for 26 hours. In this part, to prevent the growth of saprophytic fungi, cycloheximide, and bacteria growth, chloramphenicol was added to the Saburo dextrose agar medium. Diagnosis of candidiasis was cultured based on positivity. A sample of milky yeast colonies was taken and sampled. After confirmation of the colony under a microscope, it was transferred to a chromium agar culture medium and incubated in an incubator at 37 °C for 26 hours. Then, fungal species were differentiated by creating specific pigments. Ingredients of Candida chromium agar medium (CHROMagar Company, Paris, France) included 10.2 g/l of peptone, 0.5 g/l of chloramphenicol, 22 g/l of chromogenic material, and 15 g/l of agar. Its pH was set to 6.1.

Candida chromium agar medium is a differential medium for different types of Candida species such as *C. albicans*, *C. tropicalis*, *C. glabrata* and *C. parapsilosis* based on the creation of a specific pigment for each species. Thus, light green colonies of Candida albicans, blue colonies with dark brown to the purple aura of Candida tropicalis, pink colonies with the rough surface of Candida cruise, white colonies with the smooth surface of Candida parapsilosis, and dark purple colonies with pink edges and smooth surface of Candida glabrata were

considered (15). Three months after IUD placement, follow-up was performed and another cervicovaginal sample was prepared from the participants in the study, with the same method as described and sent to the laboratory. Finally, a comparison was made between the prevalence of candidal vulvovaginitis and isolated species before and three months after IUD placement.

SPSS 16 software, tests for two Correlated Proportions (McNemar Test) and T-Test were used for data analysis. P <0.05 was considered significant.

Table1. Demographic and fertility characteristics in first group and second group

Characteristics		First Group (n=70)	Second Group (n=61)	P-value
Age	≤20	12 (17.14%)	8 (13.11%)	0.098
	20-30	37 (52.86%)	31 (50.82%)	0.141
	≥30	21 (30%)	22 (36.07%)	0.082
Occupational Status	Housewife	47 (67.14%)	39 (63.93%)	0.076
	Employed	23 (32.86%)	22 (36.07%)	0.0.65
Number of Delivery	1	34 (48.57%)	27 (44.26%)	0.344
	2	28 (40%)	22 (36.06%)	0.091
	≥3	8 (11.43%)	12 (19.68%)	0.061
Number of Abortion	0	63 (90%)	59 (96.72%)	0.059
	1	5 (7.14%)	2 (3.28%)	0.055
	≥2	2 (2.86%)	0 (0%)	0.041

Results

Based on the information obtained from a pilot study on 30 people, 160 people entered the study with 95% confidence. During the study, 29 people were excluded from the study. Sixteen people were excluded from the study due to IUD withdrawal and 13 due to migration, non-referral, and termination of cooperation. Reasons for IUD withdrawal were reported in 8 patients with increased monthly bleeding duration and duration, in 2 patients with infection, and 4 patients with spontaneous IUD withdrawal. The study ended with 131 people, of which the first group (Messi IUD recipient group) consisted of 70 people, and the second group consisted of 61 people. The mean age was 29.41±3.12 years in the first group and 30.12±2.41 years in the second group. Demographic and fertility characteristics of the study population are given in Table 1.

Candidiasis was not detected in any of the participants before IUD placement. Three months after implantation, 29.57% of the copper IUD recipient group and 22.95% of the hormonal IUD group had candidiasis. The different species that these people became infected with are listed in Table 2 separately. The results showed a significant difference between the two groups in terms of candidiasis (P = 0.031).

Table2. Prevalence of Candida species in the first two groups (copper IUD recipient) and the second group (hormonal IUD recipient).

Species	First Group (n=70)	Second Group (n=61)	P-value
Albicans	14 (20%)	10 (16.39%)	0.078
Glabrata	5 (7.14%)	3 (4.92%)	0.063
Parapsilosis	2 (2.86%)	1 (1.64%)	0.060
Total	21 (29.57%)	14 (22.95%)	0.031

Conclusion

The findings indicate that the incidence of vulvovaginal candidiasis increases significantly three months after IUD placement. This increase, which was seen in previous studies, is due to changes in the microbial flora of the reproductive system. The presence of IUDs in the uterus as a foreign body and the constant secretion of copper or hormones cause an inflammatory reaction and cellular changes that lead to changes in the dominant microflora and increased Candida colonization. The increase in glabrata species is significant after IUD placement; because it can create drug resistance and pave the way for recurrent vulvovaginal candidiasis. Three months after IUD

insertion, 29.57% of people who received a copper IUD were diagnosed with candidiasis. Also, different species of Candida were observed in 22.95% of people who received hormonal IUD. Because Candida albicans is found in the vaginal microflora of 30 to 80% of asymptomatic women (27), the decision to treat asymptomatic cases requires further study and testing (28-31). The use of Candida chromium agar differential culture medium is easy, reproducible, and cost-effective (15); however, in cases such as recurrent or complicated vulvovaginal candidiasis where an accurate diagnosis is essential for successful treatment, the use of sensitive and precise molecular methods such as PCR is recommended. Finally, studies with wider dimensions and longer follow-up periods are suggested to confirm and complete the present study.

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