



Screening for Cancer Cervix in Patients Using Intrauterine Device for Long Duration

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ABSTRACT

Background: Every year, there are more and more cases of cervical cancer worldwide. Users of intrauterine devices (IUDs) have also grown because they believe IUDs to be more secure. The current study aimed to assess the association between the long-term use of Intrauterine Contraceptive Device (IUCD) and the development of cervical intra-epithelial neoplasia through cytologic and colposcopic examination of patients using IUCDs for a long period of time and to create awareness among the IUCD users for regular follow up. **Patients and methods:** Cross sectional observational study conducted in outpatient clinic and Endoscopic unit of Obstetrics and Gynecology Department and Department of Pathology at Zagazig University Hospitals. Eighty-five females who used IUCD at least 2 years were included. Age of our studied females ranged from 21 to 45 years with mean 34.24 ± 7.14 years. All women were subjected to complete history-taking, cervical smear examination and a colposcopic was collected. **Results:** Among 85 copper T IUD users, abnormal PAP smear findings were reported in 89.4% of females. Among the 6 (7%) females who underwent colposcopy, 3 (3.5%) females were normal, and 3 (3.5%) females had abnormal findings. There were no reported cases of high grade squamous intra-epithelial lesion or squamous carcinoma. Moreover, pathological examination revealed low grade squamous intra-epithelial lesion in all females with abnormal colposcopy findings (3.5%). **Conclusion:** we concluded that the use of IUD as a contraceptive method decreases the risk of the development of cervical cancer.

Keywords: Cancer Cervix, Intrauterine Devices, Colposcopic.

INTRODUCTION

After uterine cancer, cervical cancer is the second most common gynecologic cancer in women. Despite being a pre-malignant condition of the cervix, cervical intra epithelial neoplasia (CIN) is typically asymptomatic and can be identified with normal cytological screening [1].

Ralf Richart first proposed the idea of CIN in 1968, stating that all dysplasias have the potential to develop. The terms dysplasia and CIN are interchangeable. which denotes irregular cervix epithelial lining growth and development [2].

Cervical cancer typically progresses slowly over ten to fifteen years, with identifiable and treatable precursor disorders occurring first. In these

conditions, specific cervix cells develop aberrant traits, but they are not yet malignant [3].

Cervical cancer is a preventable condition due to the availability of efficient screening programs and the delivery of a preventative HPV vaccine [4].

Generally speaking, developing nations have higher rates of cervical cancer; these nations account for 85% of all cases that are reported each year; in these nations, there are up to 450,000 new instances of invasive cervical cancer annually, which results in 275,000 fatalities [5].

According to recent estimates, 373 women in Egypt lose their lives to cervical cancer and 866 women receive a diagnosis each year. In Egypt, cervical cancer is the 13th most common

malignancy among women overall and the 10th most common among those aged 15 to 44 [6].

Since the 1940s, invasive cervical cancer has been seen as a preventable disease, with a drop in both incidence and fatality rates. This is due in part to the extended pre-invasive stage of the disease and the success of treatment following the use of Papanicolaou smear. As a result, the most beneficial cervical cancer screening program ever created is cytological screening using cervical smears [7].

The identification of risk factors for cervical intra-epithelial neoplasia (CIN) is necessary because it will open up new avenues for the development and application of various interventions that may be used to identify the onset and progression of CIN [8]

Reversible, long-lasting, safe, affordable, and the most used birth control method in the world are intrauterine devices. IUDs are thought to have a variety of impacts on sperm, ovum, fertilization, implantation, and the endometrium, while its exact mechanism of action is still unknown [9].

In fact, there is insufficient data to determine if using IUCDs increases the incidence of cervical intraepithelial neoplasia **Averbach et al.** [9], thus, the goal of the current study is to determine whether or not using IUCDs over extended periods of time carries any risks. This study aimed to assess the association between the long-term use of IUCDs and the development of cervical intra-epithelial neoplasia through cytologic and colposcopic examination of patients using IUCDs for a long period of time and to create awareness among the IUCD users for regular follow up .

METHODS

Cross sectional observational study was conducted in outpatient clinic and Endoscopic unit of Obstetrics & Gynecology Department and Department of Pathology at Zagazig University Hospitals, Sharkia, Egypt in period from 15th August 2023 to 1st February 2024. Included 85 females who are currently using IUCD for long time. The study was approved by Zagazig university local ethics commission (ZU-IRB # 1089). From all patients participating in this study an informed consent was obtained. The study follows the Helsinki Declaration (1975), which is the World Medical Association's guideline of ethics for research involving human subjects.

All the included cases used the IUCD (copper IUCD) at least 2 years. Women who were previously or are currently diagnosed with malignancy or premalignant genital tract lesions,

females who have previously experienced subtotal cervical conization, patients with vaginitis, or pelvic inflammatory disease were excluded. All women were subjected to complete history-taking including age, marital status, any abnormal bleeding or abnormal discharge.

PAP smear:

The vagina was filled with a speculum. At an outpatient clinic, a cervical smear was obtained using Ayre's spatula. To obtain a sample of cells from the endocervix, the spatula was placed into the cervix's opening and rotated. In addition, a second sample was taken from the posterior fornix and the cervix's surface, or "the ectocervix," for the Papanicolaou (PAP) smear. fixing the smear for fifteen minutes with 95% alcohol on a glass slide. Slide stained with Papanicolaou stain at Zagazig University's Department of Pathology Both basic and acidic dyes are used in the Papanicolaou stain. The basic components of the cell are stained by acidic dye, while the acidic components of the cell are stained by basic dye. Three solutions containing five dyes are used in the polychromatic PAP stain.

Colposcopic examination:

The cases with abnormal result of PAP smear and cases with visible abnormal lesion were subjected to a colposcopic examination performed by the same gynecologist with the same colposcopic device and biopsy were taken from suspected area for histopathologic examination.

Steps of Colposcopic examination; Washing of cervix by saline and then inspection for any abnormal lesion and exam the vascularity. Application of Acetic Acid (AA) 5% and assess the cervix to detect any abnormal areas that appeared white lesion and assess the vascularity, extend and size of lesion, and degree of whiteness. Application of Lugol's iodine to detect abnormal areas that was iodine negative [10g of Potassium iodide (KI), 5g of Iodine, and 100ml of Distilled water], In 20 to 30 milliliters of distilled water, dissolve KI. When the iodine dissolves, add it and boil it slowly while stirring constantly. Utilizing distilled water, dilute to 100ml. Keep in the dark in an amber glass container with a stopper. Any unusual lesions were biopsied, and the samples were sent for histopathological analysis.

STATISTICAL ANALYSIS

Version 27.0 of the SPSS program (Statistical Package for Social Science) was used to computerize and statistically analyze the gathered data (IBM, 2020). The difference between the qualitative variables was calculated using the Chi-

Square test. The standard deviation (SD) or mean ± SD was used to express quantitative data. The difference between the quantitative variables in the two groups' normally distributed data was calculated using the Independent T test. When dealing with non-normally distributed data, the Mann Whitney (MW) test was utilized to determine the difference between the quantitative variables in two groups. The level statistical significance was set at 5% level (P-value) indicates significant results P < 0.05, Highly significant results <0.001.

RESULTS

Table 1; showed that the age of our studied females ranged from 21 to 45 years with mean 34.24±7.14 years. Weight of the studied females ranged from 65 to 98 kg with mean 82.93±8.92 Kg. Duration of marriage among females in the present study ranged from 3 to 23 years with median 12 years. Regarding parity, almost two thirds of them (63.5%) were 2 to 3 while 4 to 5 was reported in 22.4% of them while 14.1% had 1 parity. Among our studied females, 74.1% used IUD for 1 to 5 years, 22.4% used IUD for 6 to 10 years and only 3.5% used IUD for more than 10 years. According to the present study, 23.5% of females had no

complain. Vaginal discharge was founded in all complained females (76.5% of females) and contact bleeding in 3.5% of females. No females had pelvic pain or previous history of high-grade intraepithelial squamous lesion.

Table 2; showed that 89.4% of the cases had abnormal PAP smear findings. Most common were reactive cell alteration, moderate chronic cervicitis, calcified body and mild chronic cervicitis (43.5%, 43.5%, 37.6% & 36.4% respectively) (**Figure 1**). No cases had HG SIL or Squamous Carcinoma.

Table 3; showed that among 6 cases had done colposcopy, 3 cases were normal, and 3 cases had abnormal findings.

Table 4; showed that 3 cases with abnormal colposcopy findings showed Low grade squamous inter epithelial lesion (LGSIL) by pathology.

Table 5; showed that there were no statistical significance differences between the studied cases had SIL and cases hadn't in age, weight, duration of marriage, parity or duration of IUD use but there was a statistically significant increase in frequency of abnormal bleeding among cases had SIL compared to cases hadn't.

Table (1): Demographic data of the studied cases:

Variable		(n=85)	
Age: (years)	Mean ± Sd	34.24±7.14	
	Range	21-45	
BMI: (Kg/m ²)	Mean ± Sd	28.5±6.13	
	Range	24.06-33.91	
Gynecological history			
Duration of marriage: (years)	Mean ± Sd	12.54±5.64	
	Median	12	
	Range	3-23	
Parity:		No	%
	1	12	14.1
	2-3	54	63.5
	4-5	19	22.4
History of IUD uses			
Duration of use:	2-5 years	63	74.1
	6-10 years	19	22.4
	>10 years	3	3.5
Complain			
Complain:	No	20	23.5
	Vaginal discharge	65	76.5
	Contact bleeding	3	3.5
	Pelvic pain	0	0
	Previous history of high-grade intraepithelial squamous lesion	0	0

SD: Standard deviation

Table (2): PAP Smear results among the studied cases:

Variable		(n=85)	
		No	%
Smear:	Normal	9	10.6
	Abnormal	76	89.4
Findings:	Inflammatory changes (Mild chronic cervicitis)	31	36.4
	(Moderate chronic cervicitis)	37	43.5
	(Severe chronic cervicitis)	17	20
	Koilocytosis	5	5.9
	Low grade squamous interepithelial lesion (LG SIL)	3	3.5
	Atypical Squamous Cells of Undetermined Significance (ASCUS)	3	3.5
	Reactive cell alteration	37	43.5
	Calcified body	32	37.6
	High Grade Squamous Intraepithelial Lesion (HG SIL)	0	0
	Squamous Carcinoma	0	0

NB: Cases reported more than one finding

Table (3): Colposcopy findings among the studied cases:

Variable		(n=85)	
		No	%
Colposcopy:	Not done	79	93
	Normal	3	3.5
	Abnormal	3	3.5

Table (4): Pathology results among the studied cases:

Variable		(n=85)	
		No	%
Pathology:	Not done	82	96.5
	LG SIL	3	3.5

Table (5): Follow up & complication among the studied groups:

Variable		No neoplasia (n=82)	LG SIL (n=3)	t/M W	P		
Age: (years)	Mean ± Sd	34.09±7.2	38.33±4.16	1.01	0.31		
	Range	21-45	35-43		NS		
BMI: (Kg/m ²)	Mean ± Sd	28.5±6.13	88.33±7.64	1.07	0.29		
	Range	24.06-33.91	80-95		NS		
Duration of marriage: (years)	Median	12	12	0.55	0.58		
	Range	3-23	10-20		NS		
Variable		No	%	No	%	χ ²	P
Parity	1	12	100	0	0		
	2-3	53	98.1	1	1.9	Y	0.16
	4-5	17	89.5	2	10.5		NS
Duration:	2-5 years	61	96.8	2	3.2		
	6-10 years	18	94.7	1	5.3	Y	0.86
	>10 years	3	100	0	0		NS
Complain:	No	20	100	0	0		
	Vaginal discharge	62	95.4	3	4.6	Y	
	Pruritus	4	100	0	0		
	Abnormal bleeding	0	0	3	100		<0.001**

SD: Standard deviation t: Independent t test MW: Mann Whitney test χ²:Chi square test with yates correction NS: Non-significant (P>0.05) *: Significant (p<0.05)

** : Highly significant (p<0.05)

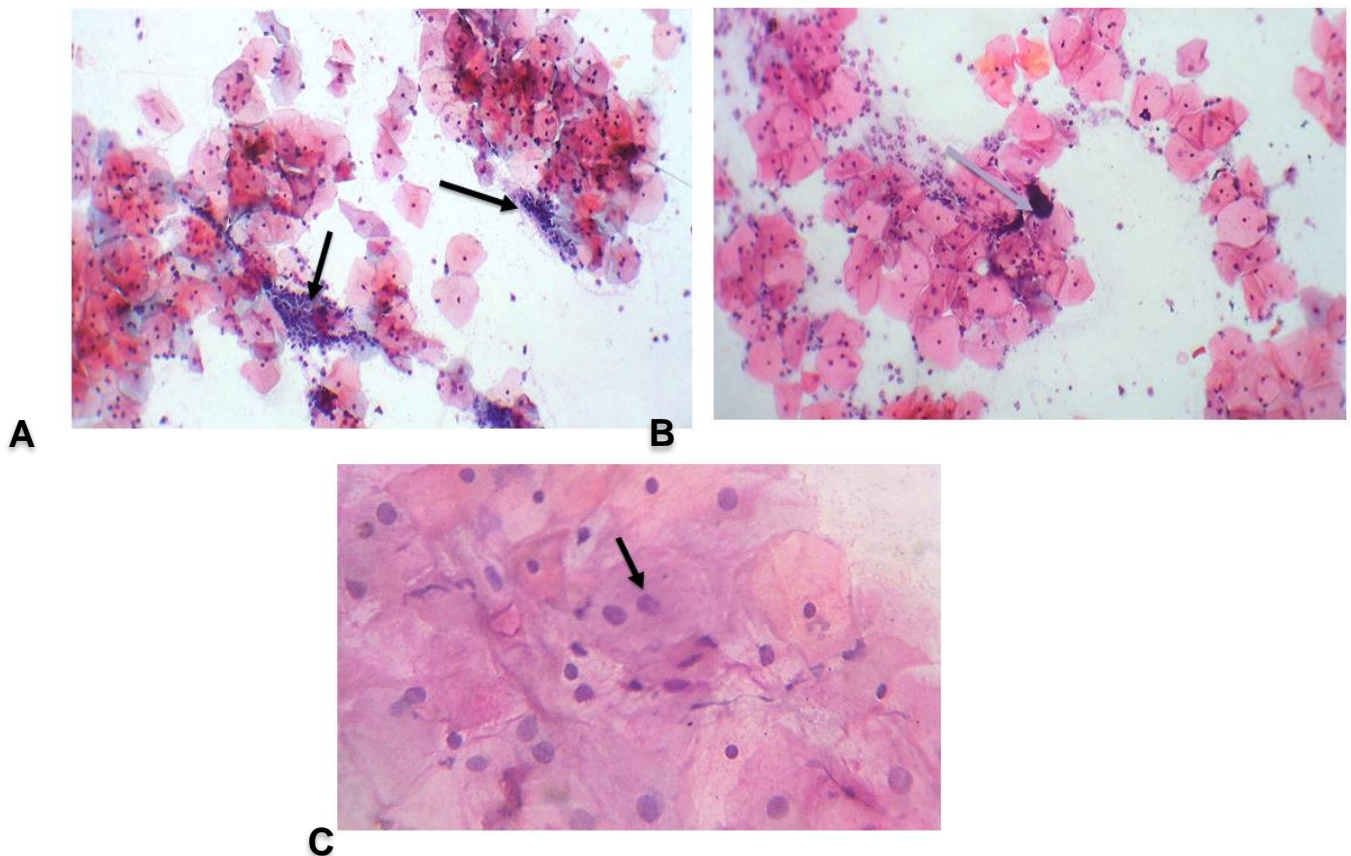


Figure 1: A mild inflammation surrounding superficial and intermediate squamous cells. arrow referred to calcified body. moderate inflammation surrounding superficial and intermediate squamous cells in women with an IUD. Arrow refers to inflammatory cells (X100). C. Inflammatory PAP with the reactive binucleation cell (arrow) (x400).

DISCUSSION

Oral contraceptives raise the risk of invasive cervical cancer, while barrier techniques lower the risk of the disease. Many contraceptive methods are linked to invasive cervical cancer [10].

In the world, the most widely used reversible method of birth control is the intrauterine device (IUD). A previous meta-analysis study by **Castellsagué et al.** [11] women who use IUDs or have previously used one have a much lower risk of cervical cancer, according to 26 research conducted globally. Lesions associated with cervical cancer progressed in around half of the other women **Curtis et al.** [12] in their study.

IUDs can increase the risk of STDs and pelvic inflammatory illness as a result of their operation. It's also been identified as a contributing factor to vaginal organ inflammation, which makes these people less likely to contract HPV infection and, thus, less likely to receive a cervical cancer diagnosis [13].

The findings of subsequent research, however, run counter to those of the previous investigations. For example, **Averbach et al.** [9] found that IUD use increases the risk of cervical intraepithelial neoplasia

(CIN) 2 in patients [9]. Numerous studies have failed to discover a connection between the usage of IUDs and a higher risk of cervical cancer [9,1213].

Through cytologic and colposcopic examination of patients who had been using IUCDs for a long time, the current study aimed to determine whether long-term use of IUCDs was associated with the development of cervical intra-epithelial neoplasia. It also aimed to raise awareness among IUCD users about the importance of routine follow-up. To obtain this aim, 85 females who used IUCD at least 2 years were included. Age of our studied females ranged from 21 to 45 years with mean 34.24 ± 7.14 years. Among our studied females, 74.1% used IUD for 1 to 5 years, 22.4% used IUD for 6 to 10 years and only 3.5% used IUD for more than 10 years.

Abnormal PAP smear findings were reported in 89.4% of females. The most reported abnormal findings were reactive cell alteration, moderate chronic cervicitis, calcified body and mild chronic cervicitis which were reported in 43.5%, 37.6%, 37.6% and 31.8% respectively.

The high prevalence of cervical inflammatory changes in the women using IUD in our study was in line with **Abd El All et al.** [14] study from Egypt, which shown that women who used IUDs were more

likely than other women to have alterations in cervical inflammatory markers.

Among the studied group, only 9 cases showed normal PAP smear while 76 cases (89.4%) were associated with abnormal findings in form of **reactive cell alteration, moderate chronic cervicitis**, calcified body and **mild chronic cervicitis** which were reported in **43.5%**, **37.6%**, **37.6%** and **31.8%** respectively.

This finding is reasonable as it is well known that one of the mechanisms of copper IUD work is to cause localized intrauterine inflammation, which destroys sperm and modifies the lining of the uterus to hinder implantation. The copper that was added to the IUD acts as a spermicidal at the uterine opening, destroying the eggs [15].

Among the abnormal PAP smear only 6 (7%) cases have epithelial cell abnormality indicating colposcopic examination in form of ASCUS (3 cases 0 and LSIL (3 cases). Normal colposcopic findings detected in 3 (3.5%) cases and 3 (3.5%) cases had abnormal findings requiring biopsy. Pathological examination of the obtained biopsy revealed low grade squamous intra-epithelial lesion in all females with abnormal colposcopy findings (3.5%).

According to the current study, none of the patients had Squamous carcinoma or high grade squamous intra-epithelial lesion.

In contrast, **Ajah et al.** study documented a greater frequency of abnormal cervical cytology among IUD users: 10.3% (16/156) [16].

No females had high grade squamous intra-epithelial lesion or squamous carcinoma in the present study.

A meta-analysis done by **Cortessis et al.** concluded that wearing an IUD lowers the risk of genital cancer linked to HPV, which in turn lowers the incidence of cancer or precancerous lesions. In fact, women who have worn an IUD may have a one-third lower incidence of invasive cervical cancer [17].

Furthermore, **Averbach et al.** comprised 85 women who, at some point during the follow-up, had utilized IUDs. Women reported using intrauterine devices at 505 of the 14,513 research visits. They concluded that IUD use may have an additional role later in the natural history of cervical cancer by preventing the development of precancerous lesions of the cervix in human papillomavirus-infected women or by accelerating the clearance of precancerous lesions that have already been established. They reported that there was no correlation between the use of IUDs and the acquisition or clearance of human papillomavirus infection [9].

Furthermore, a meta-analysis by **Castellsagué et al.** showed a statistically significant reduction in cervical cancer linked to IUD use; women who reported ever using an IUD were less likely to receive a cervical cancer diagnosis than those who had never used one [11].

Meanwhile, the idea that using a copper-IUD lowers the risk of cervical dysplasia or cancer was not conclusively supported by the data of the **Averbach et al.** study. In the **Averbach et al.** trial, there was a tendency toward a lower risk of CIN2+ among copper-IUD users. Consequently, **Averbach et al.** proposed that copper-IUDs have a slight protective effect against CIN2+ [9].

Additionally, **Ajah et al.** [16] studied Pap smear results of 156 participants on IUD and 156 non-users of modern contraception. Colposcopy was additionally performed on the participants whose abnormal cervical smear cytology results were discovered. Participants with visible cervical lesions or those with suspected lesions on colposcopy provided biopsy specimens for histopathology. According to their report, 2 (1.3%) and 7 (4.5%) of the participants who used IUDs had CIN 2 and CIN 1 respectively. Moreover, CIN 1 and CIN 2 were present in 5 (3.2%) and 1 (0.6%) of the non-users of contemporary contraception, respectively. Among all of the individuals, 4.8% had cervical neoplasia. Nonetheless, participants who used IUDs had a higher percentage of CIN-afflicted women than those who did not use contemporary contraception. The difference, however, was not statistically significant, indicating that there was no meaningful correlation between cervical neoplasia and IUD use.

The exact way in which IUDs prevent cervical cancer is not well understood. IUD use may result in long-term endocervix and ectocervix irritation. This inflammation will alter the cervix's immunological response. A study conducted by **Castellsagué et al.** [11] showed that the protective effect is unaffected by the length of IUD use. The preventive effect of an IUD is the same for women who have used it for more than 10 years as it is for those who have used it for less than a year. They put forth the notion that the implantation of the IUD causes damage to the cervix, which results in long-lasting immunological reaction and chronic inflammation.

In contrast to our research, **Tualeka et al.** study, which included six IUD users and five non-users, found that the incidence of cervical cancer was 3.33 times higher for IUD users than for non-users. The small size of the population is the reason for the discrepancy in **Tualeka et al.** [18] study.

CONCLUSION

Recommendation we more prospective studies on larger scales are required to assess the association between the long-term use of IUCDs and the development of cervical intra-epithelial neoplasia.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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