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A prospective case-control study on the association of intrauterine devices and cervical cancer risk; data from two educational centers

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Abstract

Introduction: Cervical cancer is the second most common type of cancer among women all over the world.
Objectives: This study was conducted to demonstrate the effect of intrauterine devices (IUDs) on cervical cancer and precancerous lesions development.
Patients and Methods: This study was conducted in two different hospitals in Isfahan on 200 samples, since 100 of them had results indicating cervical cancer, and the rest had no abnormal lesions. For both groups, a questionnaire was filled out for IUD users and some related risk factors such as age, parity, abortions, smoking, previous Pap smear results contained sexually transmitted diseases (STDs) infections and the contraception method.
Results: In this study, more cases of IUD use were recorded in the control group. We found that the use of natural methods did not prevent the development of precancerous lesions. In the results of the Pap smear, a large number were recorded as having a history of human papillomavirus (HPV). Additionally, a high percentage of cervical cancer patients' smoking or passive smoking. We also recorded that 53% had more than two children, while the percentages of women at the birth of their first child and who did not have an abortion were almost equal in the two groups.
Conclusion: Our analysis demonstrated that IUD use is a contraceptive method with the capability of lowering the risk of cervical cancer progression. There is also an association between HPV infection, smoking, age, the number of parity and the usage of natural birth control methods with the development of cancerous lesion development.

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Introduction

Cervical cancer is the second most prevalent cancer of women worldwide. About 2% of women before their 80 years of old are diagnosed with cervical cancer. The mean age of cervical cancer diagnosis is 52.2 years; however, the distribution of age of this disease has two peaks between 35 and 39 and 60 to 64 years old (1).

In Iran, the prevalence of cervical cancer after breast cancer has been recognized as a very important health issue. Mortality rate according to cervical cancer is being assessed at the rate of 1.2 to and 100 000 people annually (2).

Factors associated with cervical cancer are old age, residents of Asia, Africa and Latin America, low socioeconomic status, multiparty, starting sexual intercourse from low ages, multi partner women, human papillomavirus (HPV) infection, history of sexually transmitted disease (STD), smoking, and prolonged use of oral contraceptive pills (3).

Key point

In a study on 200 cervical samples (100 of them had results indicating cervical cancer, and the rest had no abnormal lesions), we found intrauterine devices (IUDs) use is a contraceptive method with the capability of lowering the risk of cervical cancer progression. There is also an association between human papillomavirus (HPV) infection, smoking, age, the number of parity and the usage of natural birth control methods with the development of cancerous lesion development.

Invasive cervical cancer is associated with many contraceptive methods, the use of barrier methods that reduce the risk of this cancer (4) and oral contraceptives increase this risk (5).

Intrauterine device (IUD) is the most prevalent reversible contraceptive method throughout the world.

A previous meta-analysis study by Castellsagué et al on 26 studies worldwide reported a significant reduction in the incidence of cervical cancer in those using

IUDs or in women who have previously used an IUD. About half of the other women had progression of cervical cancer lesions (6). This finding was also detected by Curtis et al, in their study (7).

In connection with their action, IUDs can multiply the risk of pelvic inflammatory disease and STD. It is also having been recognized as a reason for inflammation of genital organs which these patients are less likely to be involved by HPV infection and as a consequence less likely to be diagnosed with cervical cancer, these results were reached in the study conducted by Shanmugasundaram et al (8). However, the results of other studies are contradicted to the earlier studies. For example, Sara et al found that IUD use increases the risk of cervical intraepithelial neoplasia (CIN) 2 in patients (9). Many studies have not found a relationship between IUD use and an increased incidence of cervical cancer (4-9).

Objectives

This study was conducted to determine whether the use of IUD triggers the development of cancerous and precancerous lesions of cervix or not?

Patients and Methods

Study patients

In this prospective case-control study conducted from 2014 to 2018 in two different hospitals in Isfahan, 200 samples were included. The experimental group consisted of 100 patients between the ages of 18 and 49 years who were diagnosed with various precancerous lesions and cervical cancer. The control group consisted of 100 people who had no abnormal Pap smear results.

The inclusion criteria consisted of using an IUD for one to 18 months prior to the diagnosis of cervical lesions. Patients who underwent hysterectomy, or if the information in the patient's file is incomplete, were not included in this study.

All the participants consented to be in the study and ethical committee of national health ministry authorized ethical issues. A questionnaire was filled out for all participants that included information about age, type of cervical lesion, type of IUD, parity, abortions, age at birth of first child, smoking or passive smoking, previous Pap smear contained STDs infections (HPV, chlamydia, *Candida* or other), and the contraception method.

After filling out the forms, risk factors were divided separately, for example, women with cervical cancer lesions and those who smoke or passive smoking or who do not have precancerous lesions according to their history of contraceptive use, in order to prevent statistical results from overlapping.

Data analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 21 and *P* values less than 0.05 was considered as statistically significant. Chi-square method was used in order to analyze the data.

Results

Two-hundred samples from 200 women at childbearing age were included in this study. Around 79 (39.5%) of the participants were between 18-35 years old. About 121 (60.5%) patients aged between 36-50 years old were included in the study (Table 1).

Forty (20%) people used IUD devices as method of contraception, of whom only 3 (7.5 %) people used copper IUDs and the rest of them used Levonorgestrel types. Eleven (11%) patients diagnosed with cervical cancer or precancerous lesions used IUD devices as method of contraception, of whom only one (9.9 %) patient used copper IUDs and rest of them used levonorgestrel types (Table 2).

The types of cancerous lesions and the percentage of IUD use and its type are described in Table 3. This table was created only to describe the incidence rates of each type of cancerous lesions; however it is statistically not significant.

Our findings demonstrated that IUD use as a contraceptive method lowers the risk of cancerous lesion

Table 1. Age group of patients

			Groups		Total	*P* value
			Case	Control		
Age (y)	18-35	No.	37	42	79	0.47
		%	37.00	42.00	39.50	
	36-50	No.	63	58	121	
		%	63.00	58.00	60.50	
Total		No.	100	100	200	
		%	100.00	100.00	100.00	

Table 2. IUD usage and its types in the two groups

		Groups		Total	*P* value
		Case	Control		
Usage of IUD					
Yes	No.	11	29	40	0.001
	%	11.00	29.00	20.00	
No	No.	89	71	160	
	%	89.00	71.00	80.00	
Total	No.	100	100	200	
	%	100.00	100.00	100.00	
Type of IUD					
Levonorgestrel	No.	10	27	37	0.814
	%	90.90	93.10	92.50	
Copper	No.	1	2	3	
	%	9.10	6.90	7.50	
Total	No.	11	29	40	
	%	100.00	100.00	100.00	

Table 3. The percentage of intrauterine devices (IUDs) use and its type and the type of cancerous lesion

			Type of cancerous lesions					
			CIN2	CIN3	HSIL	SCC	AIS	Total
Usage of IUD	Yes	No.	4	2	2	1	2	11
		%	25.00	10.52	8.69	5.00	9.09	11
	No	No.	12	17	21	19	20	89
		%	75.00	89.47	91.30	95.00	90.90	89
Type of IUD	Levonorgestrel	No.	3	2	2	1	2	10
		%	75.00	100.00	100.00	100.00	100.00	90.90
	Copper	No.	1	0	0	0	0	1
		%	25.00	0.00	0.00	0.00	0.00	9.09

CIN; cervical intraepithelial neoplasia, HSIL; high-grade squamous intra-epithelial lesions, AIS; adenocarcinoma in situ, SCC; squamous cell carcinoma.

development ($P=0.001$).

Fifty-four point five percent of the participants were smokers or passive smokers (93% of the experimental group have a history of this). Smoking is associated with cancerous lesion development ($P=0.046$; Table 4).

Table 5 describes the number of abortions; patients who have never had an abortion are approximately equal in the two groups.

Parity in 53% of participants was more than two (Table 6). According to the data analysis, as the number of parity increases, it is more likely to be involved with cancerous lesions ($P=0.001$).

Based on Table 7, in two age groups (15-35 and over 35 years old), the percentage of women at the birth of their first child was mostly (92.5%) before 35 years.

Fifty-one percent of the participants in the experimental group had used natural contraception, since the statistics indicated that, it did not prevent the development of cancerous lesions ($P=0.043$). Around 44% of the participants used condoms as a contraceptive method (Table 8).

Twenty-five (69.4%) women from the case group, who had a history of infections on Pap smear results, had a history of HPV, while16 cases were recorded in the other group (Table 9).

Discussion

Cervical cancer is the second most common type of cancer among women after breast cancer. It was recognized as a critical health issue worldwide. In Iran, due to increase in the incidence and death caused by cervical cancer, there is an urgent need to know the causes of infection and how

Table 4. Smoking and passive smoking status

			Groups		Total	*P* value
			Case	Control		
Smoking or passive smoking	Yes	No.	93	16	109	0.046
		%	93.00	16.00	54.50	
	No	No.	7	84	91	
		%	7.00	84.00	45.50	
Total		No.	100	100	200	
		%	100.00	100.00	100.00	

Table 5. The number of abortion in patients

			Groups		Total	*P* value
			Case	Control		
Abortion	0	No.	71	73	144	0.768
		%	71.00	73.00	72.00	
	1 or 2	No.	18	19	37	
		%	18.00	19.00	18.50	
	>2	No.	11	8	19	
		%	11.00	8.00	9.50	
Total		No.	100	100	200	
		%	100.00	100.00	100.00	

Table 6. Parity number of patients

			Groups		Total	*P* value
			Case	Control		
Parity	0	No.	4	22	26	0.001
		%	4.00	22.00	13.00	
	1 or 2	No.	36	32	68	
		%	36.00	32.00	34.00	
	>2	No.	60	46	106	
		%	60.00	46.00	53.00	
Total		No.	100	100	200	
		%	100.00	100.00	100.00	

Table 7. Describing age at birth of first child

			Groups		Total	*P* value
			Case	Control		
Age at birth of first child (y)	15-35	No.	93	92	185	0.788
		%	93.00	92.00	92.50	
	>35	No.	7	8	15	
		%	7.00	8.00	7.50	
Total		No.	100	100	200	
		%	100.00	100.00	100.00	

Table 8. Contraception methods usage

			Groups		Total	*P* value
			Case	Control		
Contraception method	Tablet	No.	10	30	40	0.043
		%	10.00	30.00	20.00	
	Condom	No.	38	50	88	
		%	38.00	50.00	44.00	
	Surgery	No.	1	2	3	
		%	1.00	2.00	1. 5	
	Natural	No.	51	18	69	
		%	51.00	18.00	34.5	
	Total	No.	100	100	200	
		%	100.00	100.00	100.00	

Table 9. Results of previous Pap smear

			Groups		Total	*P* value
			Case	Control		
Previous pap smear result	HPV	No.	25	16	41	0.579
		%	69.40	72.72	70.70	
	Chlamydia	No.	1	2	3	
		%	2.77	9.09	5.20	
	Candida	No.	1	0	1	
		%	2.77	0.00	1.70	
	Other	No.	9	4	13	
		%	25.00	18.18	22.40	
Total		No	36	22	58	
		%	100.00	100.00	100.00	

to prevent it. Recently, IUD use has been identified as an associated factor in pelvic inflammatory disease. Recent studies showed that the type of inflammation that causes it, reduces the risk of infection with HPV and thus reduces the risk of cancer of the female genital organs associated with HPV. Many studies have examined the relationship between the use of IUDs and cervical cancer; however, the results were contradictory, since most of the studies were conducted outside Iran, which is the main aim of this study.

The studies conducted by Castellsagué et al and Cortessis et al, indicated that IUD use reduces the risk of genital cancer associated with HPV and therefore reduces the incidence of cancer or precancerous lesions. These results were obtained in our study as well.

Our findings highlighted that smoking is associated with precancerous and cancerous lesions development. Fonseca-Moutinho has also shown that smoking is a risk factor for cervical cancer development(10).

Multiparity has been known as a risk factor for cervical cancer progression (11). Hinkula et al concluded that multiparity is a risk factor of cervical cancer (12). Our results also are in line with this study.

From the information collected in this study, data about contraceptive methods, which indicated the presence of a large number of cervical cancer patients who did not use any method, which means that the pregnancy was naturally immunized. This result was implemented in a study at the level of a certain number of cancer cases and in a specific geographical area, hence to generalize this result; we need more studies and a larger number of patients.

Conclusion

Overall, our study showed that the use of an IUD as a method of contraception could reduce the risk of developing cervical cancer. Therefore, in women with multiple risk factors for cervical cancer, IUD use is recommended as a contraceptive.

Limitations of the study

Patients who underwent hysterectomy or in case of incomplete information of the patient file, were not included in this study.

Authors' contribution

MD, PH and ZK were the principal investigators of the study. MD, PH and ZK were included in preparing the concept and design. PH and ZK revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan of University of Medical Sciences approved this study (IR.MUI.MED.REC.1399.851). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D. thesis of Zeinab Kassab At this university (Thesis# 399155). Accordingly, ethical issues (including plagiarism, data fabrication, double publication) were completely observed by the authors.

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