

Original Article

Study of Risk Factors for Cervical Cancer A Case-Controlled Study in Isfahan-Iran

Ali Akbar Taherian¹, Eshrat Fatahi², Bahram Soleimani³

¹Department of Obstetrics and Gynecology, ²MSc Student of Obstetrics, ³Statistician, Member of Scientific Mission of Faculty of Health, Faculty of Medicine, Isfahan University of Medical Sciences (IUMS), Al-Zahra Hospital, Isfahan, Iran

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ABSTRACT

Background: Cervical cancer is the third most common malignancy of the female genital tract. The main objective of this study was to determine the risk factors for cervical cancer.

Method: This was a case-control study. From a total sample of 263 women, 87 patients with diagnoses of invasive cervical cancer comprised the case group and another 176 healthy females were in the control group. The location of research was at two oncology referral hospitals of Isfahan: Amin and Seyed Al-Shohada. Multiple logistic regression modules were used to analyze the data by SPSS-9 software.

Results: The results of the study showed that cervical cancer is related to age at first marriage (OR=5, 95% CI 1.5-16.6; P=0.008), number of deliveries (OR=3.3, 95% CI

1.2-8.8; P=0.02) and type of oral contraceptive used. In connection with duration of using oral contraceptives, the results showed that in those women who used oral contraceptives for a period of >5 years (OR=3.3, P=0.008), the mean number of sexual intercourses per week at four decades of marriage life was more in the case group compared with the control group (P=0.0001). Socioeconomic status differences were not significant. False negative Pap smear test results were about 15.5%.

Conclusion: This study identified some risk factors related to the incidence of cervical cancer i.e. younger age at the first coitus, number of intercourses per week, number of deliveries and duration of oral contraceptive use.

KEY WORDS: cervical cancer, intercourse, marriage, oral contraceptive, risk factors

INTRODUCTION

During the past several decades, the rate of cervical cancer has declined significantly in western countries though it remains one of the most common female forms of cancer in developing countries^[1].

Cervical cancer is the sixth most common malignancy of females in Isfahan. The first epidemiological study of cervical cancer, carried out in 1842 by Rigoni Stern, showed that cervical cancer is more prevalent in married women^[2]. In a study carried out in 1967, the risk factors for cervical cancer such as early marriage and delivery, number of partners and deliveries were identified as higher risk factors for cervical cancer^[3].

Use of combined estrogen and progesterone oral contraceptives (COCs) and their relation with cervical cancer is still a matter of controversy^[4-6]. Several studies have shown that oral contraceptives containing estrogen increase the risk of invasive cervical cancer, however, they have no significant relation with cervical dysplasia^[7-10]. Parazzini^[11] showed that in

women using oral contraceptives for more than two years, the risk ratio of cervical cancer is 2.5. The mechanism by which oral contraceptives affect the cervical mucosa remains unclear^[1-7]. This study was carried out to evaluate the risk factors of cervical cancer in Isfahan, Iran.

PATIENTS AND METHODS

This was a case-control study carried out between 1994-1997 in two hospitals Amin and Seyed-Al-Shohada in Isfahan, to which all patients with cervical cancer were referred. A total of 263 women were included in this study of which 87 women with histologically confirmed invasive cervical cancer. All had been referred to these two centers for treatment and follow up. The other 176 healthy women with normal pap-smears were selected as the control group. The method of sampling in the case group was a simple one and in the control group a randomized one.

A trained expert midwife interviewed both the cases and controls. A standardized questionnaire was used to obtain information. Attempts were

Address correspondence to:

Ali Akbar Taherian MD, Arjang Lane 115, Sajjad Street, 81656-66371, Isfahan, Iran.
Tel. +98-311-6613346, E-mail: md_TAHERIAN@Yahoo.com

made to validate selected items in the questionnaire by reviewing medical records. The reliability of the questionnaire was examined by test-retest procedure.

Data collection including demographic, medical, obstetrical, socio-economical and sexual histories were recorded. These data included age at first marriage (age of first sexual intercourse), age at first delivery, number of deliveries, number of marriages of the women, number of sexual intercourses per week (at first, second, third and fourth decades of marriage life), method(s) of contraceptives and duration of using COCs (Combined Oral Contraceptives Pills) and finally socio-economical status and the income of the family, level of education etc., were recorded for both groups.

SPSS-9 statistical software was used for calculations of relative risk or odds ratio (OR), 95% confidence intervals (CI) and $P < 0.05$ significant. The risks of cervical cancer were determined by comparing each group separately

with the control in the univariate analysis. Finally, statistically significant factors were included in multiple logistic regression models.

RESULTS

Mean \pm SE (Standard Error of mean) age of patients was 48 ± 1.2 and 50 ± 1.2 years in the case and control groups, respectively. Pap smear tests in those with invasive cervical cancer showed a 15.5% false negative results.

Table 1 shows the estimated relative risks (OR) of cervical cancer in relation to the study variables using univariate analysis (Chi-Square test). Multivariate analysis showed that cervical cancer is significantly related to age at first marriage < 15 years (OR=5, 95% CI 1.5-16.6; $P=0.008$), number of deliveries (parity) more than 6 (OR=3.2, 95% CI 1.2-8.8; $P=0.0001$) and those who were using COCs for more than 5 years (OR=3.6, 95% CI 1.8-7.4; $P=0.0002$). However, using COCs for 1 to 5 years was not significant when related to cervical cancer.

Table 1:

Ods Ratio(OR) and 95% Confidence Interval(CI) of the reproductive, sexual, socio-economical and educational factors for cervical cancer

Risk Factors	Case (N=87)	Control (N=176)	OR	95%CI	P value
Age of first marriage(coitus)					
≥ 19 years	6	45	1		
15-18years	38	98	2.9	1.1 - 7.4	0.020
< 15 years	43	33	9.8	3.7 - 25.7	0.00001
				X^2 for trend = 19.8	0.00001
Age of first pregnancy					
> 17 years	35	125	1		
≤ 17 years	52	51	3.6	2.1 - 6.2	0.00001
No. of pregnancy (parity)					
≤ 3	11	58	1		
4-6	36	91	2.1	0.98 - 4.4	0.052
> 6	40	27	7.8	3.5 - 17.5	0.0001
				X^2 for trend = 29.1	0.00001
No. of intercourse (coitus) per week					
≤ 3	45	149	1		
> 3	42	25	5.3	3 - 9.7	0.00001
Combined oral contraceptive pills					
Never used	45	125	1		
1-5 years	20	33	1.7	0.88 - 3.2	0.11
> 5 years	22	17	3.6	1.8 - 7.4	0.0003
				X^2 for trend = 13.2	0.0002
Poor economic status					
No	28	79	1		
Yes	59	97	1.7	1.0 - 2.9	0.043
Poor Social status					
No	26	77	1		
Yes	61	99	1.8	1.1 - 3.2	0.030
Education					
Educated	23	99	1		
Not Educated	64	77	4.6	2.0 - 6.3	0.00001

$P < 0.05$ significant

The relationship between the numbers of sexual intercourses per week at first, second, third and fourth decades of reproductive life and cervical cancer showed significant differences in all four decades ($P=0.001$, $P=0.001$, $P=0.003$, and $P=0.012$, respectively). Hence, excessive number of sexual intercourses (>3 per week), increases the risk of cervical cancer (OR=5.3, 95% CI 3-9.7; $P=0.00001$).

Excluding the confounding effect of COCs on the influence of the number of sexual intercourses on cervical cancer, first those women in each the case and the control group who were not using COCs were studied from the viewpoint of number of intercourses per week and during marital life. Following exclusion of the effect of COCs, the results showed significant differences between the two groups (OR=5.4, 95% CI 2.7-11.2; $P=0.0001$). In those women using COCs for more than 5 years the differences were significant (OR=3.4, 95% CI 1.4 - 8.2 ; $P=0.008$) (Table 2).

As a result, consumption of oral contraceptives has not been the only factor affecting the incidence of cervical cancer in our patients; rather each of the independent prognostic factors has been individually predisposing the disease.

The effect of social and economical status in urban and rural status was studied separately. After excluding the effect of confounding factors, there was no significant difference seen between the two groups ($P=0.9$, $P=0.84$, respectively). Also, a significant correlation was seen between the incidence of cervical cancer and level of education in the case group ($P=0.018$) (Table 2).

In this research, a relationship was found between the number of husband's marriages and cervical cancer ($P=0.01$). However, there was no relationship between the number of existent spouses of the husband (polygamy) ($P=0.68$) and the number of marriages of the study's women ($P=0.13$).

There was also no relationship between history of cancer in first and second rank relatives.

Table 2:

Results adjusted by multiple logistic regression analysys showing the significant risk factors for cervical cancer

Variables	Regression Coefficient	Standard Error(SE)	OR*	95%CI**	P value
Age of first marriage(coitus)					
≥19 years			1		
15-18years	0.74	0.54	2.1	0.7 - 6.1	0.17
< 15years	1.61	0.61	5	1.5 - 16.6	0.008
Age of first delivery					
<17 years(yes vs No)	0.59	0.38	1.8	0.9 - 3.9	0.12
No of pregnancy (parity)					
≤3			1		
4-6	0.22	0.47	1.3	0.5 - 3.2	0.63
>6	1.16	0.51	3.2	1.2 - 8.8	0.0001
No of intercourse (coitus) pr week					
>3 per week (Yes vs No)	1.69	0.36	5.4	1.7 - 11.2	0.0001
Combined oral cotraceptive pills					
Never used			1		
1-5years	0.73	0.42	2.1	0.9 - 2.2	0.08
> 5years	1.31	0.45	3.4	1.4 - 8.2	0.008
Poor economic status					
(Yes vs No)	0.08	0.34	1.1	0.6 - 2.2	0.79
Poor Social status					
(Yes vs No)	0.38	0.42	0.7	0.3 - 1.6	0.36
Education					
(Yes vs No)	1.01	0.43	2.8	1.2 - 6.4	0.018

*Odds Ratio; ** Confidence Interval; $P < 0.05$ significant

DISCUSSION

The mean age for invasive cervical cancer has been reported to be 46.5 and 52.2 years in Colombia and USA, respectively^[12,13]. However, Walton et al. have reported it to be 45-55 years^[14]. In our study, this mean age was 48.3 years.

Gay et al., reported a 20% false negative Pap smear result rate^[15,16] but in the current study we discovered a 15.5% false negative result rate.

Early age at first intercourse was consistently found to be a risk factor in most studies^[14,17,18,19]. The importance of early age coitus lies in the fact that intercourse introduces a carcinogenic agent to the cervical epithelium, which is most susceptible during adolescence^[20-21].

In the present study, age at first marriage (coitus) was in the cases and controls 49.5% and 18.7%, respectively, less than 15 years old. The risks showed a significant trend (OR=5; P=0.008) with decreasing age at first coitus (Table 2).

The risk of cervical cancer was higher in multiparus women and increased with number of births. Several studies have been done on the relationship between number of deliveries and cervical cancer in different countries showing a higher risk of cervical cancer with the increased number of deliveries^[14,19,22]. The current study also showed a relationship between number of deliveries (more than 6) and risk of cervical cancer (OR=3.2, 95% CI 1.2-8.8, p=0.0001) (Table 2).

Parity, besides being a marker of sexual activity may act through a hormone-mediated mechanism on one of the later stages of the carcinogenic process and, therefore, be more evident at a younger age^[23].

Many studies by WHO^[5-6], Parazzini^[11] and others^[24] on the affect of consumption of combined oral contraceptives (COCs) showed a relationship between the use of these agents and the incidence of cervical cancer. Recently completed studies in both developed and developing countries on the relationship between COCs and cervical neoplasia are inconclusive. Some of the studies provide evidence of a positive relationship, particularly for long-term usage. Results are difficult to interpret because of many methodological complexities, including potential sources of bias and confounding factors such as age at first intercourse, number of sexual partners and parity^[24]. According to the results of our study, once the duration of COCs consumption exceeded more than 5 years, the risk of cervical cancer increased (OR=3.4, CI 1.4-8.2, P=0.008).

In connection with number of sexual intercourse per week, during the all decades of marital life, the studies have shown that the risk of

cervical cancer is higher in those with higher number of sexual intercourse^[3,10,18]. In the present study, following exclusion of confounding effect of COCs consumption, number of sexual intercourse per week during marital life showed a significant relation with cervical cancer in both groups (OR-5.4; P= 0.0001) (Table 2).

Multiple marriages (multiple partners) was found to be a risk factor for cervical cancer in several studies which showed a higher number of patients than controls with two or more marriage (multypartners)^[3,18,19,20]. In our study, however, the prevalence of multiple marriage was low in both groups and no significant difference was found between them. This factor is non-existent in our society, therefore, this relationship was not significant in this study (P=0.065).

Relationship between the socio-economic status and cervical cancer is still controversial. Some researchers have shown that there is a relationship between the socio-economic status and level of education and cervical cancer^[10,18,19]. Nevertheless, others reported a negative relationship between them^[10,11].

Our findings show a relationship between younger age at the first coitus, number of deliveries and COCs used on cervical cancer.

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