ASSOCIATION BETWEEN OVARIAN CANCER RISK AND CONTRACEPTIVE METHODS- AN OBSERVATIONAL STUDY

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ABSTRACT

BACKGROUND

Ovarian cancer is the most lethal malignancy of the female reproductive system. Risk of ovarian cancer increases with age, but the rate of increase slows after the menopause. Use of contraceptives confers long-term protection against ovarian cancer. This observational study examines the correlation between ovarian cancer risks with different contraceptive methods.

MATERIALS AND METHODS

This study was conducted at Department of Obstetrics and Gynaecology, Government Medical College, Kottayam, Kerala, for a period of one year. Information was collected from 112 women diagnosed with ovarian cancer as treatment group and 336 women without ovarian cancer as control group. The Chi-square test was done to find the association of ovarian cancer risk with different contraceptive methods.

RESULTS

In the sample of 112 women with ovarian cancer, 53.6% women were using any of the contraceptive methods, whereas in the control group, only 5.1% women were using contraceptive methods. Our study found out a significant association of ovarian cancer risk with oral contraceptives and tubal ligation. There was no significant association of ovarian cancer risk with IUCD, sheath and vasectomy.

CONCLUSION

Tubal ligation and oral contraceptives reduce the risk of ovarian cancer. The dual benefits of tubal ligation need to be made aware among the public and tubal sterilisation rates have to be enhanced. Oral contraceptive pill use has to be propagated as a temporary contraceptive method due to its added advantage. We recommend future research on the association of ovarian cancer risk and contraceptive methods using large samples comparable to those done in developed countries.

KEYWORDS

Ovarian Cancer, Tubal Ligation, Oral Contraceptive Pill, Contraceptives.

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BACKGROUND

Ovarian cancer is the most lethal gynaecological cancer and is the 7th leading cause of cancer deaths in women.[1] Globally, every year 2,25,000 new cases were detected and 1,40,000 people die from the disease.[2] Lifetime risk of ovarian cancer in women is 1 in 71 and the chance of dying from the disease is 1 in 95.[3] The absence of specific symptoms, effective screening and early diagnostic methods make ovarian cancers a highly dreadful malignancy.[4] Though the occurrence and mortality of this disease is high, its cause is not fully understood. Recently, association of few factors with this cancer have been identified.[5] These are classified into three categories- protective factors (parity and use of contraceptive), risk factors (lack of birth, a history of family and age) and factors such as lactation, age at menarche and age at menopause while causal association between them and the ovarian cancer is still not proven.[6,7]

In previous researches, substantial evidence validates a decreased ovarian cancer risk associated with oral contraceptive use in developed countries.[8,9] Various studies have reported decreased risk associated with tubal ligation making this an engrained protective element for ovarian cancer.[10-12] Nevertheless, little is known about other contraceptive methods and risk of ovarian cancer in developing nations.

Regardless of the origins of ovarian cancer, associations of contraceptive methods and risk of ovarian cancer in

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developing nations are less studied.[13] In order to fill the above-mentioned research gap, the present study was conducted to examine the correlation between the risk of ovarian cancer and contraceptive methods.

OBJECTIVES

1. To study the association of duration of contraceptive usage and risk of ovarian cancer.
2. To study the association between risk of ovarian cancer and contraceptive methods.

MATERIALS AND METHODS

Study Population

This study was an observation study conducted at the Department of Obstetrics and Gynaecology (OB-GYN), Government Medical College, Kottayam. The study protocol was approved by the Regional Committee for Medical Research Ethics. The period of study was for one year from August 2015 to July 2016. Information was collected from 112 women diagnosed with ovarian cancer as treatment group and 336 women without ovarian cancer as control group. All the participants were informed about this research and written consents were obtained from each participant. The study tools included the semi-structured questionnaire, ultrasound report, tumour marker measurements and statistical analysis software (SPSS).

Inclusion Criteria of Treatment Group

Women admitted to the Department of OB-GYN who had carcinoma of ovary as defined by ultrasound and tumour markers and who were willing to participate in the study were selected.

Inclusion Criteria of Control Group

Women admitted to the Department of OB-GYN who did not have carcinoma of ovary as excluded by ultrasound and tumour markers and who were willing to participate in the study were selected as control group.

Important anthropometric details were recorded from the patients using a standard questionnaire. Methods and duration of usage of contraceptives were collected in detail.

Statistical Analysis

We calculated the descriptive statistics of the sample population and Chi-square test was carried out to study the association of ovarian cancer risk with different contraceptive methods.

RESULTS

In the sample of 112 women with ovarian cancer, 53.6% women used any of the contraceptive methods. In the control group, only 5.1% were using contraceptive methods (Figure 1). Chi-square value was 138.9 and there was significant association between contraception usages and ovarian cancer risk, which implies that the lack of contraceptive use significantly increases the risk of cancer ovary.

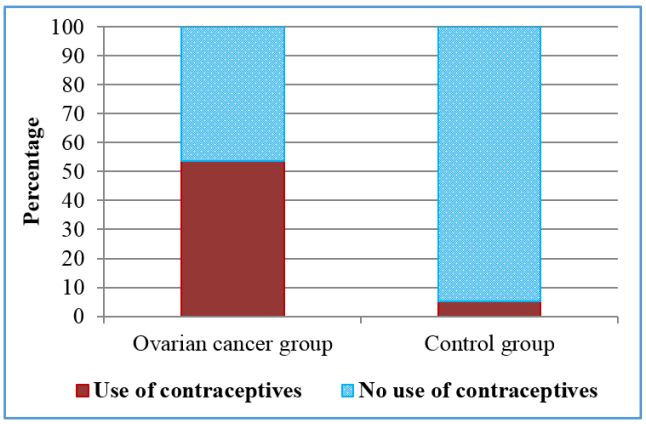

Figure 1. Distribution of Study Population According to Use of Contraception

Table 1 depicts the frequency and results of Chi-square test. In the ovarian cancer group, highest percent of women used contraceptives for less than 10 years, whereas in control group highest percentage for the duration of contraception usage falls in the range of 10-20 years (Figure 2).

Duration of Contraception in Years	Ovarian Cancer Group (Numbers)	Control Group(Numbers)	P value
<10	23	67	0.000***
10-20	11	227	
>20	18	25	
Not applicable	60	17	

Table 1. Association of Ovarian Cancer Risk with Duration of Contraceptive Usage

***Significant at 0.01, Chi-square = 174.3, odd ratio= 0.085, 95% CI= 0.034-0.212.

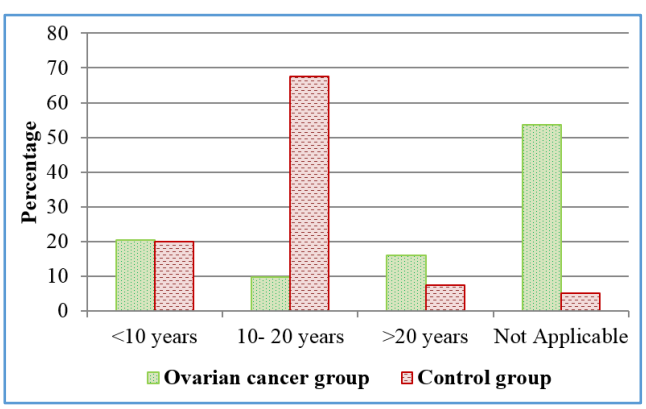

Figure 2. Distribution of Study Population According to Duration of Contraceptive Use in Years

Table 2 to 6 shows the association of ovarian cancer with various contraceptive methods. 10.7% of ovarian cancer group and 45.5% of control group women had tubal ligation. Our study reveals that there is significant relation between ovarian cancer risk and use of tubal ligation (Table 2).

Tubal Ligation	Ovarian Cancer Group		Control Group		P value
	Number	%	Number	%	
Yes	12	10.7	153	45.5	0.000***
No	100	89.3	183	54.5	

Table 2. Association of Ovarian Cancer Risk with Adoption of Tubal Ligation

***Significant at 0.01, Chi-square=43.7, odd ratio= 0.085, 95% CI= 0.034-0.212.

In the analysis of association between ovarian cancer and use of sheath, we obtained the Chi-square value as 3.1, but there is no significant association between sheath use and causation or protection against cancer ovary (Table 3).

Sheath	Ovarian Cancer Group		Control Group		P value
	Number	%	Number	%	
Yes	11	9.8	34	10.1	0.21
No	101	90.2	302	89.9	

Table 3. Association of Ovarian Cancer Risk with Adoption of Sheath

The occurrence of ovarian cancer is significantly more in group with Oral Contraceptive Pills (OCP) usage. The odds ratio indicates that when compared to people who don't use OCP, the risk of developing ovarian cancer is 0.057 times more in those who take OCP (Table 4).

OCP	Ovarian Cancer Group		Control Group		P value
	Number	%	Number	%	
Yes	5	4.5	66	19.6	0.000***
No	107	95.5	270	80.4	

Table 4. Association of Ovarian Cancer Risk with OCP Usage

***Significant at 0.01, Chi-square=43.7, odds ratio = 0.057, 95% CI= 0.017-0.193.

In ovarian cancer group and control group, the usage if Intrauterine Contraceptive Device (IUCD) is less. The Chi-square value is 0.119, but there is no significant association between the usage of IUCD and ovarian cancer risk (Table 5).

IUCD	Ovarian Cancer Group		Control Group		P value
	Number	%	Number	%	
Yes	26	20.5	64	19	0.730
No	89	79.5	272	81	

Table 5. Association of Ovarian Cancer Risk with Adoption of IUCD

Only very few of the patients' partners had undergone vasectomy in the control group, and in the ovarian cancer group, none of the patients' partners had undergone vasectomy. However, there is no statistical significant different between two groups (Table 6), which means vasectomy neither predisposes nor protects against cancer ovary.

Vasectomy	Ovarian Cancer Group		Control Group		P value
	Number	Percentage	Number	Percentage	
Yes	0	0.0	5	1.5	0.194
No	112	100.0	331	98.5	

Table 6. Association of Ovarian Cancer Risk with Adoption of Vasectomy

DISCUSSION

A risk factor is anything that changes an individual's chance of getting a disease-like cancer. Many people who get the disease may not have had any known risk factors. Even if a woman with ovarian cancer has a risk factor, it is very hard to know how much that risk factor may have contributed to the cancer. Researchers have discovered several specific factors that change a woman's likelihood of developing epithelial ovarian cancer. These risk factors don't apply to other less common types of ovarian cancer like germ cell tumours and stromal tumours.

Collaborative group on epidemiological studies of ovarian cancer reports that the ovarian cancer risk is less in those women who had used contraceptives for longer durations. Our results also showed a similar trend. Women who used oral contraceptives had a lower risk of ovarian cancer. The mechanisms underlying this noticeable reduction have not been well-defined. However, many studies confirm that ovulation with its associated disruption and subsequent repair of the ovarian epithelium can lead to the acquisition of genetic damage in ovarian epithelial cells and in turn to ovarian cancer in susceptible individuals.[14,15,16] We also found a similar result. In our study, the lower risk is seen only after 3 to 6 months of using the pill and the risk is lower as the duration of the pills usage increases. This reduced risk continues for many years even after the pill is stopped.

Tubal ligation may reduce the chance of developing ovarian cancer by up to two-thirds. Our study also showed that tubal ligation reduces ovarian cancer risk. Several mechanisms have been proposed to explain the protective effects of tubal ligation on ovarian cancer risk. Tubal ligation has been hypothesised to reduce blood flow to the ovary resulting in altered levels of hormones and growth factors, block the retrograde flow of carcinogenic or inflammatory agents from the vagina into the peritoneal cavity and induce immunity to mucins, which are over expressed in ovarian cancer.[17-21]

Many researches indicate that most ovarian cancers arise from tissues embryologically derived from the

Mullerian ducts.[22] Ovarian cancer cells are believed to originate from exfoliated endometrial cells[23] and are associated with endometriosis[24] and mutations in the ARID1A gene.[25] In contrast, many serous high-grade cancers are assumed to originate from the distal fimbrial end of the fallopian tube.[26] Tubal ligation is significantly more protective for endometrioid and clear cell cancers than for serious high-grade cancer because the location of the ligation near the ureterotubal junction prevents the retrograde transport and ovarian seeding by cells originating from the endometrium, but not the distal tubes.

CONCLUSION

Our study investigated the association between ovarian cancer and contraceptive methods including tubal ligation, OCP, IUCD, sheath and vasectomy. We used Chi-square test to estimate the association of ovarian cancer and contraceptive methods. Our study proved that use of contraceptives, duration of contraceptive use, tubal ligation and OCP had a significant association with ovarian cancer risk.

People should make aware regarding the prevalence, symptomatology, screening/diagnostic techniques, treatment modalities and prognosis of ovarian cancer. The dual benefits of tubal ligation need to be made aware among the public and tubal sterilisation rates have to be enhanced. We recommend the promotion of tubal ligation as a permanent method of contraception in those who have completed their families. Oral contraceptive pill use has to be propagated as a temporary contraceptive method due to its added advantage. We recommended further studies involving large samples comparable to those done in Western countries.

REFERENCES

[1] Gubbels JA, Claussen N, Kapur AK, et al. The detection, treatment, and biology of epithelial ovarian cancer. J Ovarian Res 2010;3:8.

[2] Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127(12):2893-2917.

[3] Ahlgren JD. Epidemiology and risk factors in pancreatic cancer. Seminars in Oncology 1996;23(2):241-250.

[4] Chornokur G, Amankwah EK, Schildkraut JM, et al. Global ovarian cancer health disparities. Gynecol Oncol 2013;129(1):258-264.

[5] Beral V, Doll R, Hermon C, et al. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. Lancet 2008;371(9609):303-314.

[6] Tsilidis KK, Allen NE, Key TJ, et al. Oral contraceptive use and reproductive factors and risk of ovarian cancer in the European prospective investigation into cancer and nutrition. Br J Cancer 2011;105(9):1436-1442.

[7] Razi S, Ghoncheh M, Mohammadian-Hafshejani A, et al. The incidence and mortality of ovarian cancer and their relationship with the human development index in Asia. Ecancermedical science 2016;10:628.

[8] Ness RB, Grisso JA, Vergona R, et al. Oral contraceptives, other methods of contraception, and risk reduction for ovarian cancer. Epidemiology (Cambridge, Mass) 2001;12(3):307-312.

[9] Tworoger SS, Fairfield KM, Colditz GA, et al. Association of oral contraceptive use, other contraceptive methods, and infertility with ovarian cancer risk. Am J Epidemiol 2007;166(8):894-901.

[10] Hankinson SE, Hunter DJ, Colditz GA, et al. Tubal ligation, hysterectomy, and risk of ovarian cancer. A prospective study. JAMA 1993;270(23):2813-2818.

[11] Rice MS, Hankinson SE, Tworoger SS. Tubal ligation, hysterectomy, unilateral oophorectomy, and risk of ovarian cancer in the nurses' health studies. Fertil Steril 2014;102(1):192-198.e3.

[12] Rice MS, Murphy MA, Vitonis AF, et al. Tubal ligation, hysterectomy and epithelial ovarian cancer in the New England case-control study. Int J Cancer 2013;133(10):2415-2421.

[13] Huang Z, Gao Y, Wen W, et al. Contraceptive methods and ovarian cancer risk among Chinese women: a report from the Shanghai women's health study. Int J Cancer 2015;137(3):607-614.

[14] Schildkraut JM, Bastos E, Berchuck A. Relationship between lifetime ovulatory cycles and overexpression of mutant p53 in epithelial ovarian cancer. Journal of the National Cancer Institute 1997;89(13):932-938.

[15] Ames BN, Gold LS. Too many rodent carcinogens: mitogenesis increases mutagenesis. Science (New York, NY) 1990;249(4972):970-971.

[16] Preston-Martin S, Pike MC, Ross RK, et al. Increased cell division as a cause of human cancer. Cancer Research 1990;50(23):7415-7421.

[17] Woodruff JD. The pathogenesis of ovarian neoplasia. Johns Hopkins Medical Journal 1979;144(4):117-120.

[18] Cramer DW, Welch WR. Determinants of ovarian cancer risk. II. Inferences regarding pathogenesis. Journal of the National Cancer Institute 1983;71(4):717-721.

[19] Whittemore AS, Harris R, Itnyre J. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II. Invasive epithelial ovarian cancers in white women. Collaborative Ovarian Cancer Group. Am J Epidemiol 1992;136(10):1184-1203.

[20] Ness RB, Cottreau C. Possible role of ovarian epithelial inflammation in ovarian cancer. Journal of the National Cancer Institute 1999;91(17):1459-1467.

[21] Cramer DW, Titus-Ernstoff L, McKolanis JR, et al. Conditions associated with antibodies against the tumor-associated antigen MUC1 and their relationship to risk for ovarian cancer. Cancer Epidemiology, Biomarkers &Prevention 2005;14(5):1125-1131.

[22] Dubeau L. The cell of origin of ovarian epithelial tumours. The Lancet Oncology 2008;9(12):1191-1197.
[23] Kurman RJ, Shih Ie M. The origin and pathogenesis of epithelial ovarian cancer: a proposed unifying theory. American Journal of Surgical Pathology 2010;34(3):433-443.
[24] Pearce CL, Templeman C, Rossing MA, et al. Association between endometriosis and risk of histological subtypes of ovarian cancer: a pooled analysis of case-control studies. The Lancet Oncology 2012;13(4):385-394.
[25] Wiegand KC, Shah SP, Al-Agha OM, et al. ARID1A Mutations in endometriosis-associated ovarian carcinomas. New England Journal of Medicine 2010;363(16):1532-1543.
[26] Vang R, Shih IeM, Kurman RJ. Ovarian low-grade and high-grade serous carcinoma: pathogenesis, clinicopathologic and molecular biologic features, and diagnostic problems. Advances in Anatomic Pathology 2009;16(5):267-282.