Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1111517
J Health Sci Med 2022; 5(4): 1124-1127

Human papillomavirus prevalence in unexplained infertile women with chronic endometritis

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Cite this article as: Ağar M, Ayar Madenli A, Gürbüz T. Human papillomavirus prevalence in unexplained infertile women with chronic endometritis. J Health Sci Med 2022; 5(4): 1124-1127.

ABSTRACT

Introduction: This study investigates unexplained infertile women with or without chronic endometritis (CE) and examines the prevalence of the human papillomavirus (HPV) in this population.

Material and Method: This study was done with a cross-sectional and retrospective method. The prevalence of HPV infection and related cases in the participants were examined. In this study, 15 infertile women with CE and 64 infertile women without CE were and analyzed from four perspectives: negative HPV, low-risk HPV, probable high-risk HPV, and the presence of high-risk HPV.

Results: The participants have mean age of 32.89 years ±3.95. High-risk HPV infection was detected in 3 (20%) and 11 (17%) of the patients with and without CE, respectively (p>0.05). The negative HPV (2 (13%) and 17 (26%)), low-risk HPV (3 (20%) and 20 (31%)), and probable high-risk HPV (7 (46%) and 16 (25%)) in infertile women with CE and infertile women had no significantly different prevalence (p>0.05). The two studied groups had no significantly different mean age, body mass index (BMI), and Infertility duration were not in (P=0.08, P=0.932, and P=0.283, respectively).

Conclusion: HPV has no significantly different prevalence in unexplained infertile women with and without CE. It is recommended that this study be repeated with more unexplained infertile women with CE.

Keywords: Human papillomaviruses, chronic endometritis, infertility, the prevalence of HPV

INTRODUCTION

Cervical cancer causes mortality due to cancer in developing countries. Infection with high-risk groups of human papillomavirus (HPV) causes cervical cancer as the second most common malignancy in the world as the third leading cause of mortality in women (1,2). More than 95% of the cervical cancers caused by HPV are one of the most common sexually transmitted infections in the world (2). The prevalence of HPV has been studied in different countries (3). Some studies have indicated an association between HPV and other cancers, such as lung, breast, esophageal, colon and rectum, and prostate cancers; however, a recurrent causal relationship between these cancers and the virus has not been shown (4,5).

Infertility is an essential psychological stress factor for couples (6,7) and has high costs for the health systems of countries and couples. Between 15-30% of the couples face infertility problems globally (8). Different factors cause reproductive dysfunction in both men and women (9,10). Many couples also suffer from infertility for unexplained reasons one of which is chronic endometritis (CE) (11-12).

Monthly change of endometrium causes menstruation, proliferation, and decidualization affected by ovarian steroids. CE is caused by infiltration of lymphocytes, higher cell density of the stroma, and plasma cells in the stromal fibroblasts, endometrial stroma, superficial mucosal edema, and asynchronous maturation of epithelial cells (13).

CE chronically causes inflammation in the endometrium leading to infertility, mostly with or without symptoms such as dyspareunia, uterine bleeding, pelvic pain, and secretions (14). It also causes poor pregnancy outcomes such as abortion and labor preterm (15). Several studies show the important role of CE in abortion and recurrent

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Received: 30.04.2022 **Accepted:** 21.06.2022

implantation failure (16-18). Hysteroscopy with biopsy predicts intrauterine inflammation well (16). CE has the approximate prevalence rate of 10-11% based on biopsies of those undergoing hysterectomies under benign gynecologic conditions (12).

Therefore, this study aimed to study the prevalence of HPV infection in infertile women with and without CE. We can design preventive strategies and appropriate and novel treatment approaches by understanding the disease pathogenesis.

MATERIAL AND METHOD

The study was carried out with the permission of Clinical Research Ethics Committee of Beykoz University (Date: 16.04.2021, Decision No: 1). All procedures were carried out by the ethical rules and the principles of the Declaration of Helsinki. Seventy-nine participants in this study visited Medistate Hospital Gynecology and IVF Clinic for infertility treatment from January 2020 to January 2021. Participants ranged in age from 23 to 40 years.

Inclusion and Exclusion Criteria

Seventy-nine participants in this study visited our hospital for infertility treatment from January 2020 to January 2021. Participants ranged in age from 23 to 40 years. The inclusion criteria were: (1) the woman between the ages of 20 and 45. The exclusion criteria were: (1) pregnant women and women in the breastfeeding period; (2) women who did not receive infertility treatment; (3) absence of diabetes, thyroid dysfunction, and systemic diseases; (4) not smoking and not using alcohol.

The study participants were divided into two groups. The infertile women had CE in the first group, and the second group included infertile women without CE. The number of participants in the first and second groups was 15 and 64, respectively. All infertility cases were unexplained, and hysteroscopy was performed on all participants. Demographical and clinical characteristics, including age, body mass index (BMI), average menstrual cycle, infertility duration, menstruation time, abortus, infertility type, pap smear results, premenstrual spotting, intermenstrual bleeding, dysmenorrhea, and menorrhagia were similar.

Laboratory Parameters

After performing a cervical canal swab (Roche Molecular Systems, Cobas PCR collection media, Inc.) for all participants, samples were tested (Cobas 4800 HPV, Roche Diagnostics, GmbH, Mannheim, Germany) for HPV DNA diagnosis and analysis of samples. In this test, the target DNA was amplified using nucleic acid hybridization and polymerase chain reaction (PCR) to identify different types of HR HPV in cervical epithelial cells. The two types, HPV-18 and HPV-16 are the critical types. This analysis makes it possible to diagnose other types of HPV in infectivity clinically significant levels.

PCR is a very widely used test tube system developed for in-vitro replication of nucleic acids. The selective amplification allows for target DNA. At the end of PCR amplification, the target DNA increases logarithmically, and more than 1 million target DNAs are generated after 30 cycles. PCR assays commonly employed in epidemiologic investigations target genetically conserved areas in the L1 gene.

Statistical Analysis

Data were analyzed, tabulated, and subjected to using the SPSS.

(version 26). The continuous data were displayed as mean±SD. At the same time, categorical data were illustrated as percentages and numbers. The Kolmogorov-Smirnov test of normality was utilized to test the normality hypothesis. The test results used proper parametric (Independent t-test) and nonparametric tests (Man Whitney and Chi-square test). A p-value of < 0.05 was regarded as statistically significant.

RESULTS

This study sample included 79 participants (15 cases and 64 control) with unexplained infertility. The participants' BMI and mean age were 23.29±2.92 and 32.89 years ±3.95, respectively. The mean duration of infertility is 3.46±1.38 years. The mean average menstrual cycle is 26.20±3.03. The mean number of menstruation time oocytes is 5.02±0.98. The HPV findings showed that low-risk HPV was found in 23 (29.1%), probable high-risk HPV was detected in 23 (29.1%), and high-risk HPV was found in 14 (17.7%). 19 (24.1%) patients detected negative HPV. **Table 1** shows the explanatory information of the variables. Descriptive characteristics of other variables omit for brevity.

Table 1. Explanatory information on the variables

Variable	N	Min	Max	Mean	SD
Age(yr)	79	23.00	40.00	32.89	3.95
BMI	79	18.20	34.00	23.29	2.92
Infertility duration (yr)	79	1.00	7.00	3.46	1.38
Average Menstrual Cycle (days)	79	2.00	29.00	26.20	3.03
Menstruation time (yr)	79	3.00	8.00	5.02	0.98
HPV		**Frequency**		**Percent**	
HPV Negative		19		24.1	
Low-Risk HPV +		23		29.1	
Probable High Risk HPV +		23		29.1	
High-Risk HPV +		14		17.7	

Min: Minimum, Max: maximum

Table 2 shows the comparison of laboratory findings of the two groups. The patients with CE as a case group and control group in terms of age had no statistically significant difference(p-value=080). The control group had higher age (33.29) than the case group (31.20). There was no statistically significant difference between the case group and controls in terms of BMI, average menstrual cycle, infertility duration, menstruation time, and abortus (p-value>0.05).

Table 2. The distinction between laboratory results of two groups

Variable	Categories	Patients with CE (n=15) (Mean±SD) or n(%)	Control (n=64) (Mean±SD) or n(%)	P value
Age(yr)		31.20±4.53	33.29±3.72	0.080**
BMI		23.72±2.89	23.19±2.94	0.932*
Average menstrual cycle (days)		25±6.45	26.48±1.32	0.990**
Infertility duration (yr)		3.13±0.99	3.54±1.45	0.283**
Menstruation time (yr)		5±1.25	5.03±0.92	0.720**
Abortus		0.06±0.25	0.12±0.37	0.616**
Infertility type				0.912**
	Primer	12 (80.0)	52 (81.3)	
	Secondary	3 (20.0)	12 (18.8)	
Pap smear results				0.922***
	Normal	10 (66.7)	45 (70.3)	
	ASCUS	2 (13.3)	10 (15.6)	
	HGSIL	1 (6.7)	4 (6.3)	
	LGSIL	2 (13.3)	5 (7.8)	
Premenstrual Spotting				0.399***
	Yes	4 (26.7)	11 (17.2)	
	No	11 (73.3)	53 (82.8)	
Intermenstrual Bleeding				0.108***
	Yes	8 (53.3)	20 (31.3)	
	No	7 (46.7)	44 (68.8)	
Dysmenorrhea				0.368***
	Yes	6 (40.0)	18 (28.1)	
	No	9 (60.0)	46 (71.9)	
Menorrhagia				0.391***
	Yes	2 (13.3)	15 (23.4)	
	No	13 (86.7)	49 (76.6)	

* Independent-Samples t-test ** Mann–Whitney U test ***Pearson Chi-Square Test

The case group and controls had no statistically significant difference infertility type, pap smear results, premenstrual spotting, intermenstrual bleeding, dysmenorrhea, and menorrhagia (P-value>0.05). **Table 3** compares HPV prevalence in two groups. The prevalence of HPV types in the two groups is not significantly different.

Table 3. Comparison of HPV prevalence in two groups

Variable	Categories	Patients with CE (n=15) n(%)	Control (n=64) n(%)	P value
HPV				0.330*
	HPV Negative	2 (13.3)	17 (26.6)	
	Low-Risk HPV+	3 (20.0)	20 (31.3)	
	Probable High Risk HPV+	7 (46.7)	16 (25.0)	
	High-Risk HPV+	3 (20.0)	11 (17.2)	

*Pearson Chi-Square Test

The **Figure** shows the tissue samples studied by the two groups and the prevalence of negative HPV, low-risk HPV, probable high-risk HPV, and high-risk HPV infection. The most prevalent in patients with CE was probable high-risk HPV +. HPV negative had the lowest prevalence in patients with CE. The most prevalent in the control group was low-risk HPV +. High-risk HPV + had the lowest prevalence in control group.

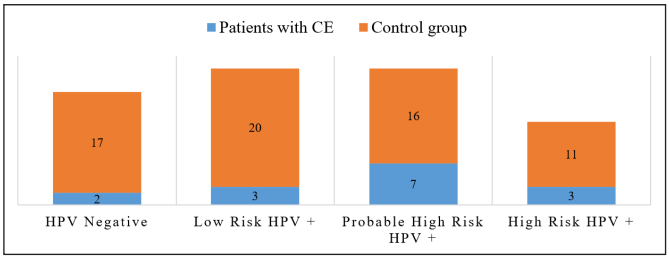

Figure. HPV infection prevalence in patients with CE and control group

DISCUSSION

The present study investigates to what extent HPV is prevalent in unexplained infertile women with and without CE. Our study showed no significantly different incidence of HPV infection between the two groups with CE and without CE. Also, it was not associated with age, BMI, average menstrual cycle, infertility duration, menstruation time, abortus, infertility type, pap smear results, premenstrual spotting, intermenstrual bleeding, dysmenorrhea, and menorrhagia.

Due to the role of HPV infection in cervical cancer, the low-risk, probable high-risk, and high-risk HPV prevalence in women in general and infertile women was studied in many research (3,6,19,20). Investigation revealed that the HPV prevalence in infertile women (21) and women with ovarian endometriosis (22). The HPV prevalence in women with CE was not studied.

In this study, 13% of women with CE had no HPV infection. This infection was not detected in 26% of women in the control group. This finding showed that the number of the infertile woman without disease in the control group was twice as much as in the case group. Low-risk HPV was detected in 20% and 31% of case and control groups, respectively. 46% and 25% in case and control groups had probable high-risk HPV, respectively. Prevalence of probable high-risk HPV was almost twice as common in infertile women with CE. 20% and 17% had high-risk HPV in the case and control groups, respectively. The prevalence of low-risk HPV and high-risk HPV was similar in both groups.

In many studies on HPV, high-risk HPV prevalence is considered the primary measure of majority (22).

According to the study's findings, the high-risk HPV prevalence in the two groups of infertile women with CE and infertile women is not significantly different.

The HPV prevalence in unexplained infertile women with and without CE for the first time was investigated. It is not possible to compare the prevalence of this infection with other studies. It is recommended that this study be conducted with a larger sample to gain more reliable results. This study's limitation is that the piece is small, and there is no access to more detailed information from the participants. The limitation of this study is that the number of patients group (the infertile women had CE) and control groups (infertile women without CE) are not enough.

CONCLUSION

The HPV prevalence in infertile women with CE and infertile women is not significantly different. The findings of this study can be used as the baseline for future studies to study the HPV prevalence in CE infertile women. It is recommended that this study be repeated with more case-patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Clinical Research Ethics Committee of Beykoz University (Date:16.04.2021, Decision No: 1).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

Financial Disclosure: The author declared that this study had received no financial support.

Author Contributions: The author declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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