

Original Article

Prevalence of cervical epithelial cell dysfunction in Papanicolaou smears reports in low-risk population referred to Imam Reza hospital

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Abstract

Background: Epithelial cell abnormality is the outcome of a viral infection. Human papilloma virus (HPV) is the main causative agent of cervical dysplasia. Cervical dysplasia caused as a consequence of infection by this sexually transmitted virus is characterized by abnormal cells on the cervix.

Various laboratory tests with varying specificity and sensitivity, have been set for diagnosis. The present study has been carried out in order to determine the prevalence rate of cervical epithelial cell dysfunction in Papanicolaou (Pap) smear reports in low risk population referred to Imam Reza hospital- Tehran- Iran from January 2019 till August 2020.

Methods: 676 women of low risk group referring to obstetrics and gynecology clinic - Imam Reza hospital- Tehran –Iran since January 2019 till August 2020 were the study cases. Information regarding presence of atrophy while examination, erosion, cervicitis, infection, Polyp, abnormal vascularity, candidiasis was collected from patients and were recorded in a check list. Patient's sample (pap smear) was collected for pathological examination. Data were analyzed by SPSS software.

Results: Pap smear examination revealed 662 out of 676 (97.5%) cases had no abnormality in cervical epithelial cells. In 12 cases abnormality was of ASCUS type (%1.77).

Conclusion: Results of Pap smear test revealed low frequency of cervical epithelial cell abnormality among low risk group. Out of the influencing factors, cervicitis, followed by erosion, abnormal vascularity and infection seem to be more common.

Keywords: Pap smear, Low risk group, Bethesda system, ASCUS, LSIL, HSIL, Cervical Dysplasia, Cervical Smear Test.

Introduction

Cervical cancer is one of the most preventable malignancies among human cancers. Infection of the uterine cervix with human papilloma-virus (HPV) is the main causative agent of cervical cancer [1]. About 15 high-risk types of human papilloma virus have been identified, which are responsible for cervical neoplasia and other related cancers [2]. Cervical cancer with worldwide distribution, though a preventable disease, is one of the leading causes of cancer death in women [1]. High risk HPV types lead to higher risk of developing cervical cancer compared to low risk types or are not being infected with HPV, at all [1]. The main characteristics of cervical dysplasia following infection with human papilloma virus (HPV) is abnormal cells on the cervix. The main screening strategy to reduce cervical cancer incidence is to detect precancerous lesions that can be treated before evolving to cancer [3]. Detection of cervical pre-cancer lesions can be achieved on the basis of cytology, implemented decades ago, or by HPV screening for women aged 30 years or older [1]. In most industrial countries cytology-based prevention programs, led to a significant reduction in the incidence and mortality from cervical cancer [1]. In other words, screening reduced the incidence of cervical cancer by at least 60%, and cancer specific mortality by 20–60% [4]. Papanicolaou (Pap) test, both conventional and liquid type, is routinely used to detect cervical epithelial cell abnormality [5]. In spite of its merits as a diagnostic and screening test, Pap test is not 100% accurate [3]. The present study has been carried out in order to determine the prevalence rate of cervical epithelial cell dysfunction in Papanicolaou (Pap) smear reports in low risk population referred to Imam Reza hospital- Tehran- Iran from January 2019 till August 2020.

Materials and Methods

Patient selection- 676 patients referring to obstetrics and gynecology clinic of Imam Reza hospital, Tehran – Iran from January 2019 till August 2020 were the study cases. The patients were included in the study on the basis of the inclusion criteria.

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Inclusion criteria: Absence of risk factors for cervical cancer including having single partnership, pap smear test performed by a particular pathology laboratory, low risk cases.

Exclusion criteria –Multiple sex partners of herself or husband, pap smear test performed by other pathology laboratories, immune-suppressed patients, patients diagnosed suffering genital wart, presence of previous epithelial cell abnormality in PAP tests performed earlier, use of vaginal lubricant, gel or any cream or having intercourse 48 hours prior to sample collection, previous positive HPV test.

Study cases- Patients' age ranged from 20 up to 79 years. All the cases were married with different number of children born by Normal Vaginal Delivery (NVD) or cesarean section or both.

Methodology- Patients were examined for the presence of infection and any macroscopic abnormality. A pap smear was collected from every patient. An expert performed the PAP test sampling and fixation throughout the study to minimize the errors. Patients were asked to get the pathological examination of the smear done from a specific laboratory.

A questionnaire containing questions regarding the age, marriage age, number of sex partners, number of deliveries and abortions, kind of contraceptives used, ... was filled by every patient. Result of pap smear and cervix outlook are the parameters considered in this study. A consent form was signed by each patient. Patients grouping and complications are presented in Table 1. SPSS software was used for statistical analysis of the data.

Results

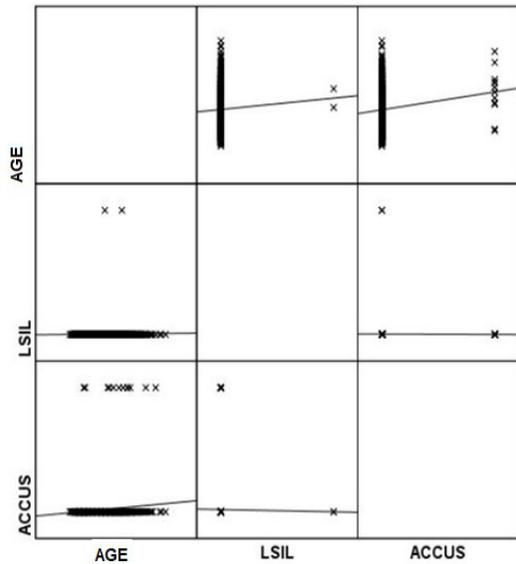
Study cases- Patients' age ranged from 20 up to 79 years with mean and median of 40 ± 13.62 and 40.69 ± 13.62 years respectively. Kolmogorov-Smirnov [6] and Shapiro-Wilk [7] tests indicate a normal distribution of the data ($p > 0.05$). All the patients were married. Mean and median of their marriage age were 20 ± 3.987 and 19.97 ± 3.987 years respectively. Their minimum and maximum marriage age were 12 and 43 years respectively. Kolmogorov-Smirnov and Shapiro-Wilk tests indicate a normal distribution of the data of this variable ($p > 0.05$). 97.5% of patients had one sex partner while 2.4% cases had married for the second

Table 1- Common complications of different age groups

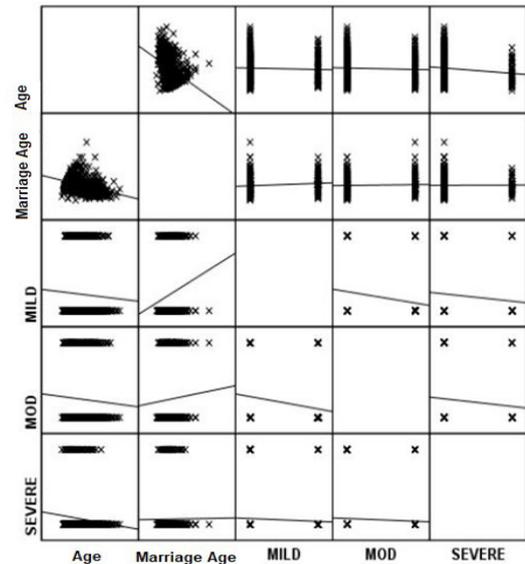
Group No.	Age Range	No. of Normal Cases	Common clinical complications						
			Cervicitis	Atrophy	Infection	Erosion	Candidiasis	Polyp	Abnormal Vascularity
I	20-29	75	53	1	13	33	8	-	1
II	30-39	79	21	1	9	23	4	3	1
III	40-49	81	17	7	15	19	17	1	1
IV	50-59	59	5	52	16	6	7	2	1
V	60-69	16	-	26	10	-	3	1	-
VI	70-79	4	4	8	1	1	2	1	-
Total	676	314	100	95	64	82	41	8	4

Table 2: Cases with Normal epithelium

Group No.	Age Range	No. in each group	Microscopic Findings of patients' samples				
			Normal PAP smear	Mild Inflammation	Moderate Inflammation	Severe Inflammation	Atrophy in PAP Smear
I	19-29	185	85	33	46	18	-
II	30-39	142	61	26	38	13	-
III	40-49	155	64	40	36	12	13
IV	50-59	131	73	20	32	6	45
V	60-69	45	30	6	6	1	35
VI	70-79	18	3	4	3	-	16
Total		676					



Scattered Diagram 1- Relationship between age and type of epithelial abnormality



Scattered Diagram 2

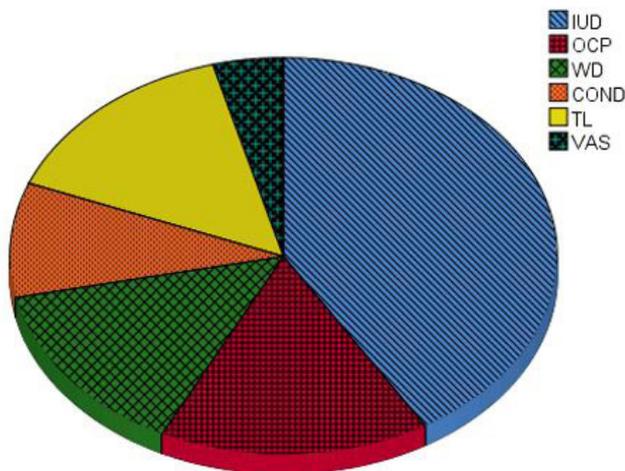


Figure 1: Type of contraceptive used by patients
 IUD= Intra Uterine Device
 OCP= Oral contraceptive pills,
 WD=withdrawal
 COND= condom
 TL= Tubal ligation
 VAS=Vasectomy

time (considered as 2 partners). One case did not answer this question. 46.4% of patients had normal cervix. According to the information obtained from the questionnaire, 163 cases had given birth to child by both vaginal (41.5%) as well as cesarean section (58.5%) and 37 cases (18.5%) had no history of delivery. Maximum and minimum normal vaginal delivery were 8 and 0 respectively. 77 cases had delivery one year after first intercourse, while 2, 56, 17, 7, 3 and 1 cases delivered their first child one and half, 2, 3, 4, 5 and 6 years after the first intercourse, respectively. Total number of abortions reported was 170 out of 676 cases. Microscopic examination of pap smears revealed 662 out of 676 (97.5%) cases had no abnormality in cervical epithelial cells (Table 2). Microscopic findings of patients' sample are also illustrated in Table 2 revealing that 14 (2.07%) patients showed epithelial cell abnormality in their pap smears: In 12 cases abnormality was of ASCUS type (1.77%). No patients had HSIL, 2 patients had LSIL, one in each age groups of 30-39 and 40-49 years. 16.1% of cases suffered cervical

atrophy, 2 cases had vaginosis and 2 patients were infected with Candida. The commonest complication in this group was cervicitis which was observed in 6 cases, erosion was observed in 4 cases and infection due to Candidiasis in 2 cases, atrophy was observed by direct observation in 1 case. Out of these 14 cases, 3 had normal vaginal examination. The mean of ASCUS cases was 4.44 that was found in age group of 60-69 years. The marriage age was the only influencing variable on mild form ($p < 0.05$) with about 9% increase in it.

Different types of contraceptives used by patients are presented in Figure I. η^2 test was used to find out if the type of contraceptive used and inflammation caused while collecting sample for Pap smear are co-related. The statistical analysis using Phi test with Phi correlation coefficient of 0.175 and Cramer correlation coefficient of 0.087 indicates a non-significant relationship.

χ^2 test was used to find out if the type of delivery and inflammation caused while collecting sample for Pap smear are co-related. The value of 5.36 indicates that there is non-significant relationship.

To find out if the number of deliveries and inflammation caused while collecting sample for Pap smear are co-related, χ^2 test was used. Pearson Chi-Square test with 44 degrees of freedom is equal to 67.53 which is significant at 5% level. Their co-relation on the basis of Phi test with Phi correlation coefficient of 0.350 and Cramer correlation coefficient of 0.175 indicates a significant correlation.

To find out if the number of abortions and inflammation caused while collecting sample for Pap smear are co-related we used χ^2 test. Pearson Chi-Square test shows a non-significant relationship. Their co-relation on the basis of Phi test with Phi correlation coefficient of 0.162 and Cramer correlation coefficient of 0.081 is non-significant.

To find out the relationship between patients' age and inflammation due to sample collection for PAP test using η^2 relation coefficient, shows a weak significant relationship.

To find out the strongest relationship for a particular variable, scatter diagram - 1 is drawn. According to the scatter diagram - 1, age is the only determinant factor for ASCUS ($p < 0.05$) and no other factor is so effective. Also, by a single year increase in the age, the rate of ASCUS increases up to 8%; which is equal to 1.083 times its probability.

Thereby, chance of infection increases by 8 percent for single unit increase in the age. 19.1% of all patients had mild inflammation, 23.8% had moderate and 7.2% suffered severe form of inflammation. Scatter diagram – 2 is drawn to study the correlations between the studied variables and to determine which variables are related. Logistic regression outcome reveals none of the studied variables has any effect on LSIL as the significance value of all the studied variables is more than 0.05. 50.1 percent had normal pap smear.

Discussion

Cervical cancer with an estimated 604,000 new cases and 342,000 deaths is the fourth cause of cancer death worldwide in 2020 [8]. Globally, 528 000 new cases of this cancer were diagnosed in 2012; of these, about 85%, occurred in less developed parts of the world and 266000 women died of it throughout the world. In another word, 231000 women who lived in low- to middle income countries died of this type of cancer. While, only 35 000, or just 1 in 10 women suffering from cervical cancer lived and died in high-income countries [3]. Cervical cancer is one of the preventable cancers involving primary (HPV vaccine) and secondary (screening) preventive measures. More than 30% of women of low middle income countries (LMICs) had received HPV vaccination programs compared with less than 80% of high-income countries [8]. In Iran, this viral infection and its resultant disease has also been reported and nation-wide screening program has been performed since 1980s. In the present study, out of 676 study cases, 97.8% had normal epithelial cell and 46.45 percent cases had normal cervix examination. Only 2.2% of our patients suffered from signs related to epithelial cell abnormality.

According to Majidi et al. (2016) incidence of cervical cancer is low in Iran [9]. Crosbie et al. (2013) estimated average prevalence rate of cervical infection with HPV at a given point, and at any time is about 10-4%, with higher prevalence rate (16-9%) in women younger than 25 years. [2]. In contrast to Crosbie et al s findings, our findings indicate a lower incidence rate as our patients are chosen from low-risk population i.e. almost all are of ASCUS type. In Iran, like many other countries, routine screening for cervical cancer is based on the microscopic examination of smears collected from the cervical mucosa, performed by conventional Pap smear test. Screening by cervical cytology in United States in the mid20th century reduced mortality from squamous cell cervical cancer [10]. More so, it led to increased number of women being identified with HPV-negative, ASCUS-cytology results [11], as is the case in the present study. Whilst cervical cancer, once the most frequent cause of cancer death in women, now ranks 14th for cancer deaths [11]. High-quality screening with cytology (Pap testing) has markedly reduced mortality from squamous cell cervical cancer, which comprises 80–90% of cervical cancers [9-11].

Screening interval that varies between countries, is an important issue. Cervical screening is performed every 3 years in the United States, New Zealand, and Norway, while its interval is 5 years in Denmark, Finland, and the Netherlands [12]. In Iran, annual cervical cancer screening program was performed for age range of 20 to 65 years. Since 2017, it changed to 3 year intervals for women at the age of 30 to 59, following three consecutive normal results. Sawaya and Smith-McCune (2007) suggested that molecular DNA test performed for HPV

diagnosis every 10 years for women at the age of 35 years and more is preferred as DNA HPV test is a novel and effective screening method [13]. There is no doubt that such screening programs reduce the incidence and mortality rate of cervical cancer, globally [13].

Starting age of screening also varies in different countries. Screening starts at the age of 25 in United Kingdom, France, Italy and Portugal and at the age of 21 in the United States and Canada [12]. Cervical cancer screening in countries like Finland, Korea, the Netherlands and China begins at the age of 30 to 35 years [12]; while according to National Health service, cervical screening program is to be done every three years for women between the age of 25 - 49 years and every five years for women past 50 [14]. In spite of previous recommendation of annual or biannual cervical screening, as it seems that annual screening is of little benefit and leads to increased cost (15), some guidelines in Great Britain, recommended every three years for women under 50, and every five years for those who have passed fifty [14]. In the present study, patients' age ranged from 20 to 79 years. Based on the fact that the incidence of cervical cancer in Iran is low compared to other geographical areas, we recommend three-year interval for healthy women with no history of cytological screening.

Conclusion

Worldwide, cervical cancer is a common and deadly cancer among women. Screening programs and effective treatment of precancerous lesions are available to treat the patients. In most cases, slow progression of precancerous lesions, are accompanied by abnormal cells which are detected in Pap test. The cervical screening program using the Pap smear procedure has an influencing role in reducing the incidence and mortality rate of invasive cervical cancer in many countries, including Iran. The incidence of cervical cancer is low in Iran although its mortality is remarkable. In Iran, cervical cancer screening program was performed annually in the age range of 20 to 65 previously. Since 2017 screening is performed for women at the age of 30 to 59 at 3 year intervals after three consecutive normal results.

Conflict of interest

Authors declare no conflict of interest.

Acknowledgments

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