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Persistant inflammatory Pap smear follow-up by colposcopic examination and biopsy to detect pre invasive and invasive changes of the cervix

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Background

Inflammatory Pap smear results are the most commonly observed by gynecologist during their practice. However persistent inflammatory can obscure malignant cells in the pap smears and early diagnosis of pre invasive and invasive cervical changes. In this study we followed up those cases of persistent inflammatory Pap smear by colposcopy and biopsy to detect pre invasive and invasive malignant changes in cervix.

Objectives

This study was conducted to detect the pre invasive and invasive changes of the cervix in women who have persistent inflammatory Pap smear and treat them earlier.

Method

A prospective observational study was carried out from Augus 2018 to August 2019 at Maternity Teaching Hospital, Erbil city, Kurdistan region on 200 women presented with different symptoms. Pap smear, colposcopy and biopsy were done for suspicious areas and sent for histopathological examination.to diagnose any pre invasive and invasive changes.

Results

In the biopsy results the highest proportion (42.1%) of the women aged less than 30 years had inflammatory changes while the highest proportions of those aged ≥ 50 years had ASCUS/CIN (60%). The proportions of ASCUS/CIN was also high in the age groups 30-39 and 40-49 years, but low in the age groups less than 30 years (p=0.047).

Conclusions:

There is high percentage (51.1) of pre invasive changes among women with persistent inflammatory Pap smear, where majority of them aged between 30-39 years.

Key words

Persistent inflammatory Pap smear, Atypical Squamous cell of undermined significance, cervical intraepithelial neoplasia, cancer, colposcopy.

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Introduction:

Cervical cancer which is squamous cell carcinoma of the uterine cervix is one of a very common but easily detectable and preventable malignancies[1]. This type of cancer in its early phases of progression can be completely treated, because the malignant cells are still restricted to the surface of the cervical tissues[2]. World Health Organization (WHO) reports shows that nearly 80% of deaths from cervical cancer were from developing countries, this is due to lack of screening programs and low level of awareness among women[3].

Cervical cancer, the invasive lesions, which involves beyond the cervical tissues, is developing from a primary lesion called preinvasive cancer or cervical intraepithelial neoplasia[4]. Human papilloma virus infection is the most serious factor enhancing the cervical epithelial cells to undergo malignant changes[5]. In other hand chronic inflammation in the cervix is accountable for speeding up the turn over and mitotic rate of the cervical cells and may induce their change to malignant cells[6,7].

Cytological examination and screening through Pap smear and colposcopy is aimed to detect preinvasive lesions of the cervix and it is regarded to be a very good tool to detect presence of inflammation in the area[8].

Repeated inflammatory Pap smear results are the most commonly observed by gynecologists during their practice[9]. In developing countries usually inflammatory Pap smear are not subjected to further smears. However persistent inflammation can obscure malignant cells in the Pap smears and early diagnosis of preinvasive and invasive cervical cancer[6]. In this study we tried to evaluate further investigation of cases of persistent inflammatory Pap smear by colposcopy and biopsy to detect preinvasive and invasive malignant changes in cervix.

Material and Methods:

A prospective observational study was carried out on 200 women attending gynecological outpatient department of Maternity Teaching Hospital and private gynecology clinics in Erbil city of Kurdistan Region, Iraq between the periods from August 2018 to August 2019. The study was approved by Kurdistan Board for Medical Specialties (KBMS) ethics and scientific committee.

Inclusion criteria

Non-virgin women between the age 20 to 65 attending gynecologic outpatient with different complaints like: abnormal vaginal discharge, post coital pain or bleeding, chronic pelvic pain, abnormal menstruation, vulvar itching and post-menopausal bleeding.

Exclusion criteria

Women below the age of 20 and above 65 years, pregnant woman, postpartum period, virgin, obvious cervical growth, prior cervical cancer, pre-invasive diseases of the cervix and total hysterectomy.

A signed informed consent had been obtained from all participants after explaining the information leaflet to them. Then a questionnaire was filled which contained a thorough medical history and examination including obstetric and gynecological examination of all the participants. After that the procedures (Pap smear & colposcopy) were explained to all the participants. Two days before Pap smear the patients should avoid vaginal douching, vaginal medicines, spermicidal foams, creams or gels and sexual intercourse, because they may obscure abnormal areas. In cases where the result of their Pap smears was inflammatory, we gave anti microbial treatment to the participant and her partner for at least seven days and were advised them to do sexual abstinence or barrier contraception during the period of treatment. By the end of the 4th week the Pap smear was repeated. Those participants whose Pap smears were still inflammatory were subjected to colposcopy examination. A thorough colposcopy examination by applying 5% acetic acid on cotton swabs for 1 to 2 minutes on the cervix. Then the transformational zone of the cervix was checked for acetowhite areas and then punch biopsy was

taken from these areas and sent for histopathological examination for confirming or excluding any pre invasive and invasive changes of the cervix

Statistical analysis

Data were analyzed using the Statistical package for Social Sciences (SPSS, version 22). Chi square test of association was used to compare proportions. Fisher's exact test was used when the expected count of more than 20% of the cells of the table was less than 5. A p value of ≤ 0.05 was considered statistically significant.

Results

Two hundred women participated in the study. Their mean age $\pm$ SD was 35.12 $\pm$ 8.16 years, ranging from 20 to 58 years. The median was 34 years. The highest proportion of the women (46.5%) aged 30-39 years, and only 5% aged $\geq$ 50 years as presented in Table 1. The majority (75%) of the sample came from urban areas. Regarding the socio-economic status, 66.5% of the women were of low socio-economic status. Only 5.5% of the women were smokers, and 0.5% were alcohol drinkers.

Table 1. Basic characteristics of the studied sample.

	No.	**(%)**
Age (years)		
20-29	47	(23.5)
30-39	93	(46.5)
40-49	50	(25.0)
≥ 50	10	(5.0)
Residency		
Urban	150	(75.0)

Rural	50	(25.0)
Socio-economic status		
Low	133	(66.5)
Medium	51	(25.5)
High	16	(8.0)
Smoking		
Yes	11	(5.5)
No	189	(94.5)
Alcohol intake		
Yes	1	(0.5)
No	199	(99.5)
Total	200	(100.0)

The majority of the women (92%) presented with vaginal discharge, 90.5% presented with pelvic back pain, and 71% presented with pain during coitus. The other symptoms are presented in Table 2.

Table 2. Presenting symptoms of the women.

Symptoms*	**No.**	**% (n = 200)**
Vaginal discharge	184	(92.0)
Pelvic back pain	181	(90.5)
Pain during coitus	142	(71.0)
Inter-menstrual bleeding	75	(37.5)
Heavy period	75	(37.5)
Post-coital bleeding	73	(36.5)
Postmenopausal bleeding	8	(4.0)

*A woman may present with more than one symptom.

Cervical inspection showed that the 92% of the women had abnormal discharge, 77.5% had redness, 66% had congestion, 65% had erosion, and 64% had bleeding. The other findings are presented in Table 3.

Table 3. Results of cervical inspection.

Findings	No.	% (n = 200)
Abnormal discharge	184	(92.0)
Redness	155	(77.5)
Congestion	132	(66.0)
Erosion	130	(65.0)
Bleeding	128	(64.0)
Nabothian follicle	29	(14.5)
Ulcer	23	(11.5)
Irregular surface	23	(11.5)
Polyp	1	(0.5)
Growth	1	(0.5)

Table 4 shows that 94.5% had inflammatory changes by the first PAP smear which shows also that 3% of the women of the whole sample were normal. Another PAP smear was done later for 189, its results showed that 92.6% had inflammatory changes and 4.8% were normal. It is evident in the table, according to colposcopy that 8% of the women were normal, but according to the biopsy (done for 161 women), 28% found to be normal.

Table 4. The study findings.

	No.	(%)
PAP 1 results		
Normal	6	(3.0)
Inflammatory	189	(94.5)
ASCUS	3	(1.5)
CIN1	2	(1.0)

Total	200	(100.0)
PAP 2 results		
Normal	9	(4.8)
Inflammatory	175	(92.6)
ASCUS	4	(2.1)
CIN1	1	(0.5)
Total	189	(100.0)
Colposcopy findings		
Normal	14	(8.0)
Abnormal	161	(92.0)
Total	175	(100.0)
Biopsy results		
Normal	45	(28.0)
Inflammatory	38	(23.6)
ASCUS	7	(4.3)
CIN1	61	(37.9)
CIN2	10	(6.2)
Total	161	(100.0)

The highest proportion (42.1%) of women aged less than 30 years had inflammatory changes while the highest proportion of those aged ≥ 50 years had ASCUS/CIN (60%). The proportion of ASCUS/CIN was also high in the age groups 30-39 and 40-49 years but low in the age group less than 30 years ($p = 0.047$). No significant association was detected between the biopsy findings and the following variables: duration of marriage ($p > 0.999$), socio-economic status ($p = 0.179$), smoking ($p > 0.999$), family history of cancer ($p = 0.488$), current contraception method ($p = 0.125$), and past contraception method ($p = 0.234$).

Table 5. Biopsy result by patients' characteristics.

	Normal	**Inflammatory**	**ASCUS/CIN**

	No.	(%)	No.	(%)	No.	(%)	p
Age							
< 30	12	(31.6)	16	(42.1)	10	(26.3)	
30-39	20	(26.3)	14	(18.4)	42	(55.3)	
40-49	10	(27.0)	7	(18.9)	20	(54.1)	
≥ 50	3	(30.0)	1	(10.0)	6	(60.0)	0.047*
Duration of marriage (years)							
< 5	2	(28.6)	5	(71.4)	0	(0.0)	
5-9	11	(30.6)	8	(22.2)	17	(47.2)	
10-14	11	(25.6)	10	(23.3)	22	(51.2)	
≥ 15	21	(28.0)	15	(20.0)	39	(52.0)	> 0.999*
Socio-economic status							
Low	31	(28.4)	22	(20.2)	56	(51.4)	
Medium	11	(28.9)	14	(36.8)	13	(34.2)	
High	3	(21.4)	2	(14.3)	9	(64.3)	0.179*
Smoking							
Yes	2	(22.2)	2	(22.2)	5	(55.6)	
No	43	(28.3)	36	(23.7)	73	(48.0)	> 0.999*
Family history cancer							
Yes	13	(22.8)	13	(22.8)	31	(54.4)	
No	32	(30.8)	25	(24.0)	47	(45.2)	0.488*
Current contraception method							
Traditional	22	(29.7)	18	(24.3)	34	(45.9)	
POP pills	1	(100.0)	0	(0.0)	0	(0.0)	
COC pills	1	(25.0)	2	(50.0)	1	(25.0)	
IUCD	5	(29.4)	2	(11.8)	10	(58.8)	
Condom	3	(15.0)	2	(10.0)	15	(75.0)	
Others	0	(0.0)	3	(42.9)	4	(57.1)	
No contraception	13	(34.2)	11	(28.9)	14	(36.8)	0.125*

Past contraception method							
Traditional	17	(32.7)	12	(23.1)	23	(44.2)	
POP pills	0	(0.0)	1	(25.0)	3	(75.0)	
COC pills	7	(28.0)	7	(28.0)	11	(44.0)	
IUCD	5	(17.2)	6	(20.7)	18	(62.1)	
Condom	6	(27.3)	4	(18.2)	12	(54.5)	
Provera	1	(14.3)	5	(71.4)	1	(14.3)	
Others	1	(25.0)	1	(25.0)	2	(50.0)	
No contraception	8	(44.4)	2	(11.1)	8	(44.4)	0.234†
Total	45	(28.0)	38	(23.6)	78	(48.4)	

*By Fisher's exact test. †By Chi square test.

Discussion:

Inflammatory Pap smear is regarded the most common results of gynecologist reports. These results usually alert the gynecologist to follow up the patient because many of them could proceed to the malignant changes which could be preventable if diagnosed in its early intra epithelial stages[10]. In our study the most common complains that patients were suffering from was vaginal discharge (92%). This proportion is significantly higher than what is reported by Shanmugham et al where they reported 69% of their study sample to have this symptom.[11]

On initial Pap smear 94.5% of our patients' revealed inflammatory changes, this is much higher than results of Shanmughan et al (84.5%) and Bhutia K et al (24%).[11,12] This high percentage may be due the fact that our study sample is of patient who are seriously ill when they attend private clinic and tertiary specialty hospital.

Repeated Pap smear after course of treatment of patients with inflammatory changes showed persistent inflammation in 92.6%. This indicates that in spite of treatment still the results are not significantly responding. In a study done in India the persistent inflammatory Pap smear was reduced from 24.3% to 8.6%.[10] The results of Shanmughan et al showed reduction of persistent inflammatory Pap smear to half (84.5%-42.6%).[11] This difference between the results is mostly due to poor adherence of patients to the course of treatment. In other hand the treatment also may be needed to be more specific to the pathology to improve the condition.

In our study, out of 175 cases of persistent inflammatory Pap smear 92% had abnormal colposcopy this is incredibly higher than results of Bhutia et al (53.3%), whereas it is nearly

similar to that of Dasari P et al, where they reported abnormal colposcopy to be about 90.7% of cases.[6,12]

Women with persistent inflammatory Pap smear (175 patients) were underwent colposcopy. Biopsy was done for suspected cases during colposcopy (161 patients). Results of biopsy showed that 44.1% of them had CIN. These results two times more than the results found by Bhutia et al (16.67%).[12] Again this higher percentage of CIN in our study may be due to the inclusion of seriously ill patients in the study.

Conclusions:

Inflammatory Pap smear results are significantly high in our patient (94.5%). In the other hand, prevalence of pre malignant and borderline changes is very high among women with persistent inflammatory Pap smear, CIN 44.1% and ASCUS 7%. The largest number of our patients (42 patients) who had CIN/ASCUS where aged from 30-39 years old.

Recommendation:

Strict colposcopy and biopsy are mandatory for all case of persistent inflammatory Pap smear result.

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