Comparison of Diagnostic Methods in Detection of Squamous Cell Abnormalities in Iranian Women with Abnormal Pap's Smear Test and Associated Demographic and Issues

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KEYWORDS

ABSTRACT

Background & Objective: Premalignant lesions of cervix have increased dramatically in recent years. Early diagnosis and management of abnormalities have an effective role in preventing the invasion of the disease and also in timely treatment. This study aimed to compare diagnostic methods in the detection of squamous cell abnormalities with abnormal Pap smear test.

Methods: This cross-sectional study was performed on 1000 women with abnormal Pap smears in 2007-2018. Sampling was performed with simple method. All samples were subjected to an immediate assessment of colposcopy and histopathology if suspected. The checklist included demographic information as well as symptoms, cytopathology, colposcopy and histopathology findings. Data analysis was performed using descriptive and statistical analysis (*P*<0.05).

Results: A significant relationship between histopathology and Pap smear findings was found (*P*=0.009), also there was a significant correlation between histopathology and colposcopy findings (*P*=0.001). However, there was no significant relationship between clinical symptoms and histopathology findings (*p*=0.8). Sensitivity , specificity , positive and negative predictive value of Pap smear were 43%, 65.9%, 75.4%, 32.2% and of colposcopy were 74.7%, 39.5%, 75%, 39.1%, and of clinical symptoms were 72.6%, 28.1%, 71.1%, 29.7%, respectively.

Conclusion: Pap smear findings have the appropriate diagnostic accuracy in comparison with colposcopy and histopathology findings for screening and diagnosis of squamous intra-epithelial lesions. Also, there was higher sensitivity of colposcopy compared with Pap smear to detect cervical lesions. Therefore, it is advisable to use these methods simultaneously.

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Introduction

One of the most common cancers among women around the world is cervical cancer (1). Nearly 80% of cervical cancer cases occur in developing countries (2). Cervical cancer is the second most common cause of cancer-related death among women worldwide, with over 500,000 new cases diagnosed annually and about 50% mortality rate in Asia (3).

Based on a report by the National cancer registry center of Iran, the mean age specific incidence rate of cervical cancer was 2.5 in 100,000 individuals (range: 0.4 (Zanjan, Iran) - 4.1 (Fars, Iran)) and this cancer was the 2nd most common gynecological cancer among Iranian women (4,5).

Today, fortunately the prevalence of cervical cancer in Muslim countries, including Iran is less but the mortality rate is significant (6).

According to several studies, more than 80% of Iranian known cases of cervical cancer had been positive for Human papillomavirus (HPV) (7). HPV oncogene is a known risk factor for the development of cervical cancer (8), but there are other risk factors such as: smoking, promiscuous sexual behavior, sexually transmitted diseases, multi partnership, partner's sexual behavior, nutrition, socioeconomic level, genetic and patient's hormonal and immunological status (9). Thus, cervical cancer can be prevented by using the HPV

vaccine, HPV screening test and Papanicolaou (Pap) smear (cytopathology) (10).

Due to the long latency period of cervical cancer and presence of screening methods and effective therapeutic approach to premalignant lesions, cervical cancer is a preventable malignancy. Common screening tests include a Pap smear, colposcopy, and cervical biopsy (11).

The Pap test is the most common and cost-effective screening method for detection of cervical cancer. This method is effective in reducing the prevalence of this cancer and the associated morbidity and mortality rates among women (12). The most widely used approach to describe Pap smear or cytopathology results is the Bethesda System (13).

Since the sensitivity and specificity of the Pap smear test are lower than colposcopy (14), all patients with abnormal Pap smear cytology results should undergo colposcopy examination (15).

To identify patients who require treatment, colposcopy and a guided biopsy remain a critical diagnostic step for evaluation of women with squamous intraepithelial lesions (16).

By comparing various methods of screening, the strength and weakness of each method can be recognized, and by improving the strength and resolving the weaknesses, the efficiency of methods can be increased. In addition, by comparing the results of different methods, the necessity of performing additional tests can be discovered. Therefore, choosing the preferred screening and diagnostic methods, leads to reduce aggressive and expensive procedures (17).

The results of studies demonstrate that the sensitivity of colposcopy in the detection of squamous cell abnormalities is higher compared with Pap smear and has the highest diagnostic accuracy for high grade squamous cell abnormalities compared to low grade squamous cell abnormalities (15,16).

Despite the benefits of each screening method, none of these methods seems to be effective in screening and early detection of cervical cancer alone. Therefore, learning more about the benefits and limitations of any method is necessary (18).

The gold standard method for definite diagnosis of cervical intraepithelial lesion is a histopathology examination of cervical lesion biopsy (19).

Many issues are found in the screening programs. There is a lack of comprehensive and reliable statistics about the epidemiological aspects of the disease, the predisposing factors and clinical findings. The diagnostic and therapeutic interventions are found very costly for the health care system. In addition, the complications and the mental distress of the disease are destructive for patients and their families. Therefore, due to the long incubation period of cervical cancer, it is necessary to consider effective preventive programs and an appropriate approach for early screening and diagnosis of premalignant lesions. It is also important to ensure about the accuracy and efficiency of these

methods globally and to consider appropriate methods for follow-up of the patients who are found with abnormalities on screening tests (20). It has led to the implementation of the national guidelines on revision policy.

The purpose of this article was to compare the diagnostic methods in the detection of squamous cell abnormalities in women with abnormal Pap Smear test.

Materials and Methods

This study is a cross-sectional comparative study and is conducted in accordance with the approved guidelines with the ethical code of IR.QUMS.REC.1396.8 from the Ethics Committee of Qazvin University of Medical Sciences (QUMS). The study was performed on 1000 women with abnormal Pap smear test results referring to Kowsar Academic Hospital during April 2007 to March 2018. Sampling was carried out with simple method. The inclusion criteria for entering the study included healthy, non-pregnant women who were married, had abnormal Pap smear test results, and their biopsy and colposcopy findings were completed. Exclusion criteria included incomplete cases, women who have had previous medical, therapeutic interventions of the cervix (such as cryotherapy), and previous cervical surgery, genital warts and cervical stenosis.

The number of sample size according to the prevalence of 5% (21) of ASCUS (Atypical Squamous Cells of Undetermined Significance) was considered as 1000.

Sampling was carried out by using a simple method. In this work, after obtaining permission from the university's research Deputy, the information about the patients with abnormal Pap smear were collected by the pathology department of Kowsar Teaching Hospital.

The details of patient information collected is as follows: Demographic data (Age, level of education, smoking, parity, marriage age, socioeconomic status and patient's age at first pregnancy), clinical findings (Vaginal discharge, vaginal bleeding, post coital bleeding and spotting), Pap smear cytology (Inflammation: Mild, moderate, severe. ASCUS, ASC-H, LSIL and HSIL), colposcopy findings (Acetowhite, abnormal vascular pattern (mosaism) and cervical ulcer) and histopathology findings (Cervicitis, CIN I (LSIL), CIN II and CIN III (HSIL)). All information was recorded on a checklist. In this study, the conventional Pap smear was used. All slides with abnormal results were re-evaluated by a pathologist based on last Bethesda's recommendation (13).

Colposcopy findings of individuals with abnormal Pap smear results were extracted from the patient records. Then cervical biopsy slides of patients with abnormal Pap smear and colposcopy results were collected from the pathology archives of the Hospital and examined by a pathologist. The pathologist was blind to the results of cytology when reporting histology slides. Also, if further investigation was needed, new sections of the paraffin block were prepared.

The data were analyzed using descriptive and analytic statistics (Chi-square test, logistic regression) using SPSS 16 (SPSS Inc., Chicago, IL., USA). The sensitivity, specificity, positive and negative predictive values of various diagnostic methods were calculated ($P<0.05$).

Results

The age range of the participants was 18-78 years. The findings of Table 1 show the absolute and relative frequency of demographic characteristics in the studied samples.

Table 1. Demographic characteristics in participants

| Variables		Number	Percent
Age	18-30	209	20.9
	31-43	416	41.6
	44-56	265	26.5
	57<=	110	11
Marriage age	15>	334	33.4
	15-24	366	36.6
	25-34	199	19.9
	35<=	101	10.1
Gravida	0	72	7.2
	1	183	18.3
	2	299	29.9
	3	240	24
	4	134	13.4
	4<	72	7.2
OCP use	yes	533	53.3
	no	467	46.7
Smoking	yes	-	-
	no	1000	100

Table 2. Absolute and relative frequency of different diagnostic methods findings in participants.

| Variables		Number	Percent
Clinical data	no	276	27.6
	Vaginal discharge	367	36.7
	Vaginal bleeding	357	35.7
Pap smear	cytology		
Inflammation	mild	392	39.2
	moderate	368	36.8
	severe	240	24
Squamous cell abnormalities	ASCUS	518	51.8
	ASC-H	175	17.5
	LSIL	193	19.3
	HSIL	114	11.4
Colposcopy	Normal	294	29.4
	acetowhite	337	33.7
	Vascular Pattern	174	17.4
	Ulcer	195	19.5
Histopathology	Cervicitis	291	29.1
	CIN1	644	64.4
	CIN2	51	5.1
	CIN3	14	1.4

Table 2 shows the absolute and relative frequency of clinical symptoms, Pap smear, colposcopy, and histopathology findings (Figure 1-8).

The findings of Table **3 show** a significant correlation between Pap smear findings and biopsy results (P=0.001) and between colposcopy findings and biopsy results (P=0.001). The highest percentage of ASCUS (302 cases and 51.9%) in Pap smear was related to the CIN I reported in the histopathology.
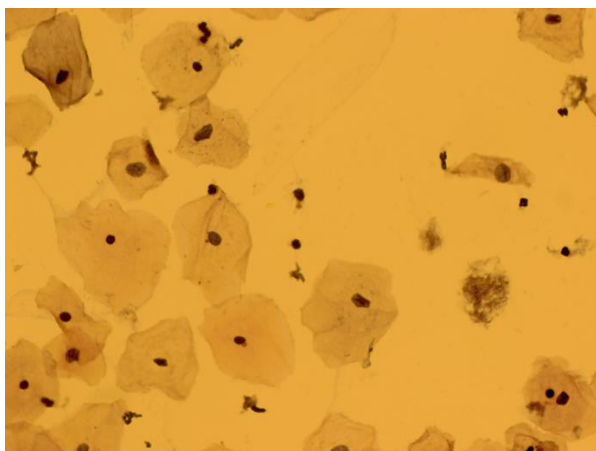

Fig. 1. ASCUS. Cells with enlarged nuclei, hyperchromatic chromatin, and small perinuclear halo without well-defined, enhanced rim (Papanicolaou, x400(blue arrows)).
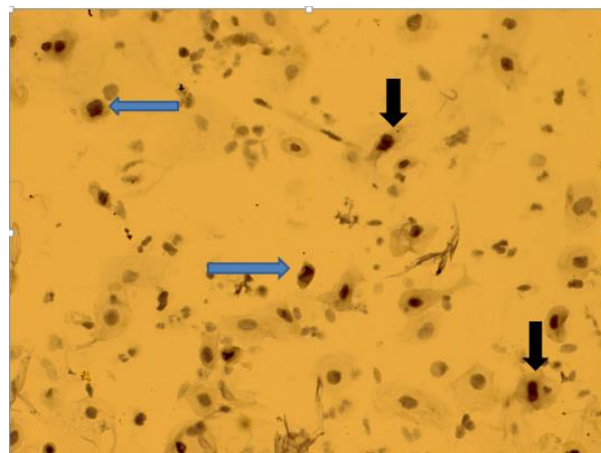

Fig. 3. ASC-H and koilocytic changes. Immature cells with high N/C ratio and nuclear hyperchromasia and irregularity. Koilocytes showing large defined perinuclear halos, binucleation, and slight nuclear atypia, with smudged chromatin. (Papanicolaou, x400(blue and black arrows)).
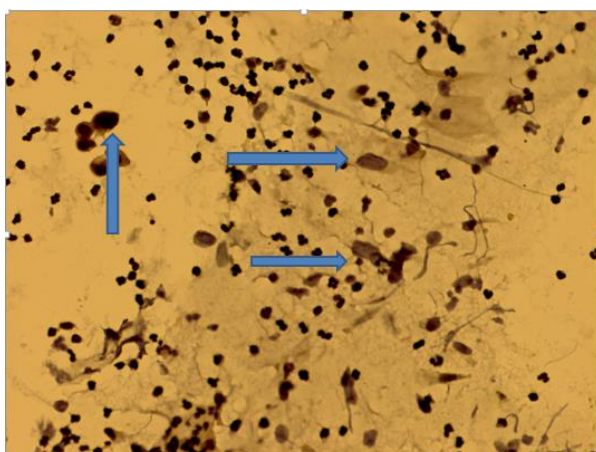
Fig. 2. ASC-H. Immature cells with high N/C ratio and nuclear hyperchromasia and irregularity. (Papanicolaou, x400(blue   arrows)).
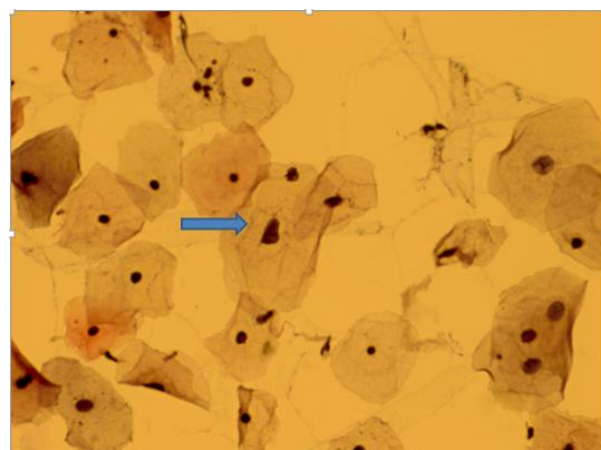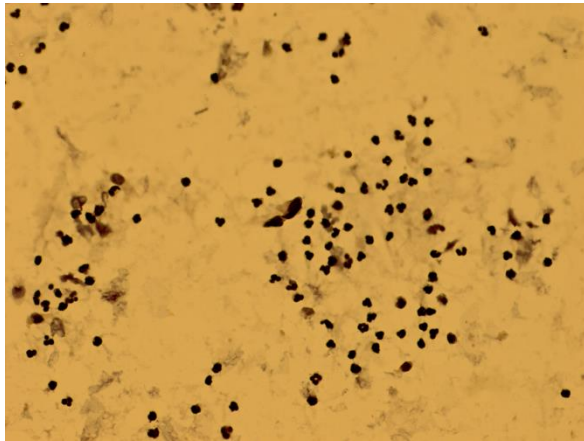

Fig. 4. LSIL. Squamous cells with hyperchromatic nuclei and perinuclear halos (Papanicolaou, x400(blue arrows))
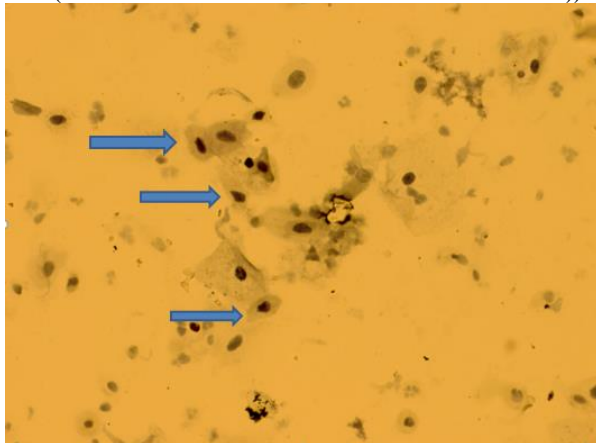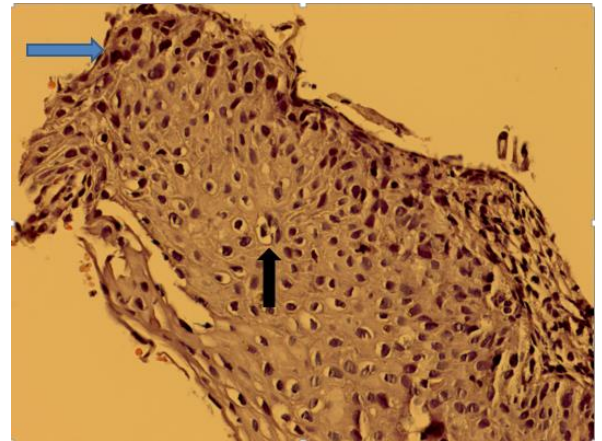

Fig. 5. Squamous cells with hyperchromatic nuclei and perinuclear halos (Papanicolaou, x400   ).
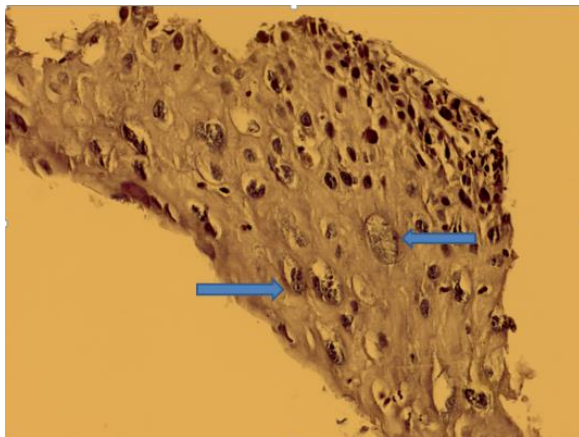
Fig. 6. HSIL. Single of immature cells with high nuclear to cytoplasm ration, hyperchromatic nuclei, and scant cytoplasm (Papanicolaou, x400(blue arrows)).

Fig. 7. LSIL and koilocytic changes. Cells with enlarged nuclei, coarse chromatin, irregular nuclear membrane , cytoplasmic halo and binucleation (H & E, x400(blue and black arrows)).

Fig. 8. HSIL. Cells with enlarged nuclei, coarse chromatin, irregular nuclear membrane , loss of polarity and nuclear hyperchromasia extending to the superficial third of the epithelium.(H & E, x400(blue arrows)).

Table 3. Investigation of the relationship between pathology with cytology, colposcopy findings and clinical signs among participants

Biopsy	Cervicitis		CIN1		CIN2		CIN3		Total	P-value
	percent	number	percent	Number	percent	Number	percent	Number	Total Number	
Pap smear(squamous cell abnormality)									518	
	65.9	192	51.9	302	35.4	18	42.8	6	175	0.001>
-ASCUS	18.9	55	13.5	101	29.4	15	28.6	4		
-ASC-H	10.3	30	23.3	152	17.6	9	14.3	2	193	
-LSIL	4.9	14	11.3	89	17.6	9	14.3	2		
-HSIL									114	
Colposcopy										
-Ulcer	22	64	18.1	117	17.6	9	35.7	5	195	
-Acetowhite	26.8	78	36.2	233	43.1	22	28.6	4	337	0.001>
-Vascular pattern	11.7	34	19.2	123	25.5	13	28.62	4	174	
-Normal	39.5	115	26.5	171	13.7	7	0.3	1	294	
Clinical data										0.1
-no	28.1	82	27.7	179	23.5	12	21.4	3	276	

| Vaginal discharge -Vaginal bleeding | 41.9 | 122 | 34.1 | 219 | 41.1 | 21 | 35.7 | 5 | 367 |
| | 29.8 | 87 | 38.1 | 246 | 35.4 | 18 | 42.9 | 6 | 357 |

Also, in the correlation between histopathology and colposcopy findings, the most acetowhite changes were related to CIN1 (233 cases and 36.2%) in the histopathology.

Table 4 shows that with increase in the grade of atypical squamous cells in Pap smear cytology results, the grade of cellular abnormality also increases in biopsy results (*P*=0.009). Also the presence of a cervical lesion in colposcopy was associated with an abnormality in the biopsy (*P*=0.001).

The results of Table 5 show that colposcopy had higher sensitivity (74.7%) and Pap smear had higher specificity (65.9%) compared with two other methods.

Table 4. Relation of pathology with other diagnostic methods in participants.

Histopathology	No intra squamous cell lesion		Intra squamous cell lesion		P-value
	%	N	%	N	
Pap Smear					
ASCUS	67.8	404	32.2	192	**0.009**
others	75.5	305	24.5	99	
Colposcopy					
Normal	60.9	179	39.1	115	0.001>
Abnormal	75.1	530	24.9	176	
Clinical data					
No	70.3	194	29.7	82	0.8
Yes	71.1	515	28.9	209	

Table 5. Sensitivity, Specificity, Positive and Negative Predictive values of Clinical Data, Cytology and Colposcopy Compared with Histopathology in participants

	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE
COLPOSCOPY	74.7	39.5	75	39.1
CLINICAL DATA	72.6	28.1	71.1	29.7
PAP SMEAR	43	65.9	75.4	32.2

Results in Table 6 show that there was a significant relationship between age and clinical symptoms (*P*=0.03). As age increased, clinical symptoms became more frequent. There was a significant relationship between marriage age and biopsy results (*P*=0.01). As the marriage age increased, the positive biopsy results for malignancy were more prevalent.

The results of logistic regression showed that there was no significant relationship between clinical symptoms with Pap smear, colposcopy and biopsy findings after adjustment of demographic variables (age, marriage age, parity, and OCP use) ((*P*=0.23), CI: (0.63-1.11)).

The results of logistic regression showed that there was a statistically significant relationship between the results of Pap smear and biopsy findings before (*P*=0.016, OR=1/42), (CI: 1.06-1.9)) and after ((*P*=0.015, OR=1/43), CI: (1.07-1.9)) adjustment.

Logistic regression results showed that there was a significant relationship between the results of colposcopy and the biopsy before and after adjusting the demographic variables. Before ((*P*=0.000, OR=1/9), (CI: 1.4-2.5)) and after ((*P*=0.000, OR=2/0), (CI: 1.4-2.6)) adjusting. Therefore, the results indicate that colposcopy diagnostic accuracy is high in detecting cervical squamous cell abnormalities. Above findings was somewhat similar to results of paper entitled "Variability study between Pap smear, Colposcopy and Cervical Histopathology" written by Dr Shahida Akhter *et al.*

Thus, the above results indicated that the Pap cytology smear and colposcopy have a sufficient diagnostic power in identifying cervical squamous cell abnormalities. The diagnostic accuracy of clinical symptoms was low.

Table 6. Evaluation of the relationship between demographic variables and different diagnostic methods results in participants

	Histopathology		Colposcopy		PAP Smear		Clinical data			
	No intra squamous cell lesion	Intra squamous cell lesion	Normal	Abnormal	ASCUS	others	No	Yes		
Age **18-30** **31-43** **44-56** **57<=**	67(%32.1) 119(%28.6) 74(%27.9) 31(%28.2)	142(%67.9) 297(%71.4) 191(%73.1) 79(%71.8)	66(%31.6) 105(%25.2) 90(%34) 33(%30)	143(%68.4) 311(%74.8) 175(%66) 77(%70)	120(%57.4) 248(%59.6) 169(%63.8) 59(%53.6)	6.۴۲) 89(% 16(%40.4) 96(%836.2) 51(%46.4)	64(%30.6) 12(%29.8) 4 55(%20.8) 33(%30)	14(%69.4) 5 29(%70.2) 2 21(%79.2) 0 77(%70)		
P value	0.7		0.08		0.2		0.03		0.2	0.7
OCP Use **yes** **no**	147(%31.5) 144(%27)	320(%68.5) 389(%73)	126(%27) 168(%31.5)	341(%73) 365(%68.5)	287(%53.8) 249(%53.3)	246(%46.2) 218(%46.7)	135(%28.9) 141(%26.5)	332(%71.1) 392(%73.5)		
P value	0.1		0.1		0.7		0.2		0.7	0.1
Gravida **0** **1** **2** **3** **4** **4<**	22(%30.6) 58(%31.7) 83(%27.9) 74(%30.8) 33(%24.6) 21(%29.2)	50(%69.4) 125(%68.3) 216(%72.2) 166(%69.2) 101(%75.4) 51(%70.8)	19(%26.4) 45(%24.6) 90(%30.1) 84(%34.6) 34(%25.4) 23(%31.9)	53(%73.6) 138(%75.4) 209(%69.9) 157(%65.4) 100(%74.6) 49(%68.1)	40(%55.6) 102(%55.7) 184(%61.5) 149(%62.1) 79(%59) 42(%58.3)	32(%44.4) 81(%44.3) 115(%38.5) 91(%37.9) 55(%41) 30(%41.7)	16(%22.2) 45(%24.6) 88(%29.4) 71(%29.6) 35(%26.1) 41(%29.2)	56(%77.8) 138(%75.4) 211(%70.6) 169(%70.4) 99(%73.9) 51(%70.8)		
P value	0.2		0.2		0.7		0.6		0.7	0.2
Marriage age **15>** **15-24** **25-34** **35<=**	118(%35.3) 87(%23.8) 57(%28.6) 29(%28.7)	216(%64.7) 279(%76.2) 142(%71.4) 72(%71.3)	91(%27.2) 115(%31.4) 56(%28.1) 32(%31.7)	243(%72.8) 251(%68.6) 143(%71.9) 69(%68.3)	200(%59.9) 223(%60.9) 113(%56.8) 60(%59.4)	134(%40.1) 143(%39.1) 86(%43.2) 41(%40.6)	108(%32.2) 95(%26) 44(%22.1) 22(%28.6)	226(%67.7) 271(%74) 155(%77.9) 72(%71.3)		
P value	0.01		0.5		0.8		0.06		0.8	

Discussion

We studied 1,000 patients with abnormal Pap smear results in Kowsar Academic Hospital (Obstetrics and Gynecology Hospital in Qazvin, Iran) from April 2007 to March 2018. With longer duration and the larger number of participants compared with previous studies, the results of current study could be more reliable than other similar researches (15,16,22).

Most of the subjects belonged to the age group of 33 to 44 years old, this finding was similar to other studies, since most women in studied populations belong to this age group (15,23).

The most common chief complaints were vaginal discharge and vaginal bleeding, respectively. Which was similar to other studies. This is due to the inflammatory and premalignant lesions of the cervix (16,24,25).

None of the patients were smoker and this was in accordance with the gender and cultural characteristics of the country. Therefore, the effects of smoking on other variables could not be verified. Approximately half of the subjects took OCP (46.4%), which was similar to other studies and indicated the current attitude toward OCP consumption in the study community (25,26).

The most commonly reported result of Pap smear was ASCUS with a frequency of 596 (59.6%). This is similar to other studies, since the inflammatory and non-malignant lesions can mimic squamous intraepithelial lesions due to conspicuous ambiguous reactive cellular changes.

Therefore, in order not to miss the suspected premalignant cellular changes, ASCUS diagnosis was more prevalent than other squamous intraepithelial lesions (16,27,28).

In the present study, the most commonly reported colposcopy finding was Acetowhite changes with frequency of 337 (33.7%) cases. These results are different from other studies.

The vascular pattern abnormalities were more frequent in other studies, since the abnormal vascular pattern was seen in low grade squamous intraepithelial lesions and Acetowhite change was seen in both low and high grade squamous intraepithelial lesions (14,29).

The most commonly reported histopathology finding in our study was CIN I with a frequency of 644 cases (64.4%), which was significantly higher than other studies. The reason for this difference is the smaller sample size of other studies and this fact that Kowsar Hospital is a referral center (14,29).

The results of this study show a significant correlation between histopathology and Pap smear findings ($P<0.05$). Thus, with the increase in cellular atypia grade in Pap smear, the degree of anomalies in histopathology results is increased. Also, the results of this study show that there was a significant relationship between Pap smear and histopathology results before ($P=0.016$, OR=1/42, CI: 1.06-1.9) and after ($P=0.015$,

OR=1/43, CI: 1.07-1.9) adjustment of demographic variables. The findings above were compared with Ramzi *et al.* and Savitha *et al.* findings. Therefore, the results indicated that Pap smear diagnostic accuracy is high in detecting cervical squamous cell abnormalities (16,30).

The results of this study also showed a statistically significant relationship between histopathology and colposcopy ($P<0.05$). The presence of abnormal lesion in colposcopy was associated with an increased squamous abnormality in histopathology. Logistic regression results showed that there was a significant relationship between the results of colposcopy and histopathology findings before ($P=0.000$, OR=1/9, CI: 1.4-2.5) and after ($P=0.000$, OR=2/0, CI: 1.4-2.6) adjusting the demographic variables. The findings above are similar to Savitha *et al.* and Akhter *et al.* study results (16,31).

The results showed that colposcopy diagnostic accuracy was high in detecting cervical squamous cell abnormalities. Pap smear and colposcopy methods both have a high accuracy in detecting suspected lesions of the cervix. These results are supported by another similar study (16).

This study shows that ASCUS in Pap smear results with a frequency of 51.9% was associated with CINI in histopathology. Also, vascular pattern changes in colposcopy with a frequency of 19.2% were associated with CIN I in histopathology. Since ASCUS is indicative of atypical squamous cells of undetermined significance, this suggests that they are part of the squamous cell abnormalities or are due to reactive changes such as radiation, medication, infection, etc. Therefore, the findings above indicated that the reported results are consistent in each of the two methods and if histopathology is introduced as a gold standard and reference method, Pap smear findings are able to properly detect the cases (19).

Compared with similar studies, the sensitivity, specificity, and positive predictive value of colposcopy in this study was equivalent to other researches and its sensitivity was within the maximum range of other studies and its specificity was modest. In different studies, the sensitivity of this method varied from 45% to 97% and its specificity varied from 19% to 90% (14,32,).

The high sensitivity of colposcopy in the present study is similar to previous studies, and the high diagnostic accuracy of this screening method for detecting abnormal cervical lesions is confirmed. The low specificity obtained was similar to other studies. This fact could lead to increased referral rates for biopsy if colposcopy was used alone.

In most of the studies conducted in this regard, the specificity of colposcopy was lower than that of Pap smear, and for this reason various studies suggested to perform colposcopy simultaneously with Pap smear to detect cervical lesions (14,32).

The sensitivity and specificity of Pap smear was in the range of other studies. In several similar studies, the sensitivity of this method was 11% to 99% and its specificity was 14% to 97%. This difference between studies suggests the effect of underlying factors on Pap smear results and it was necessary to review the preparation methods and reports of Pap smear (10, 14).

The results of the Ramsey *et al.* study shows that the Pap smear test had a high sensitivity (77.3%) to detect abnormal lesions with high grade cellular atypia. Thus, it could be considered as an effective screening test (30).

On the other hand, the results of the present study showed a sensitivity of 43% for Pap smear to detect abnormalities of squamous cells, including lesions with low and high grade cellular atypia, but had a high positive predictive value (75.4%). This suggests that, although the Pap smear test could not distinguish between high and low grades of atypia, but it could correctly recognize the true positive cases.

The Pap smear sensitivity in the present study was relatively low. As a screening method for diagnosis of cervical lesions, it was necessary to use other methods or to correct the factors that were destructive. This indicates the need for multiple consensuses to upgrade Bethesda's reporting system to reduce diagnostic errors.

In a study conducted by Karimi Zarchi *et al.*, the sensitivity and specificity of Pap smear were 18.2% and 98.5% respectively, and colposcopy was the preferred method for screening of cervical cancer (15).

For clinical manifestations, there was a high sensitivity compared to other studies (32,33). However, it is due to the high prevalence of clinical symptoms including vaginal discharge and vaginal bleeding in women with inflammatory, pre-malignant, and malignant cervical lesions. Therefore, this method did not have a strong diagnostic accuracy (31).

In the study of Savitha *et al.*, colposcopy had the highest sensitivity for detecting CIN2 and had also the highest false positive predictive value and minimal specificity ($P<0.05$). The results of this study showed that colposcopy had a high sensitivity of 74.7% and had a specificity of 39.5%, which was similar to that of Savitha *et al.* In the present study, this may also be due to over-estimation and over diagnosis (16).

The results of the studies showed that sensitivity of colposcopy in the detection of squamous cell abnormalities was higher compared with Pap smear and had the highest diagnostic accuracy for high grade squamous cell abnormalities compared with low grade squamous cell abnormalities (15,16).

Similar to other studies, a significant relationship between age and clinical manifestations was found. As age increased, the clinical symptoms also increased in patients ($P=0.05$). These facts may be due to cultural differences, more sexual activities, an increased risk of infection and exposure to oncogenes. There was also a direct relationship between the marriage age and the incidence of malignant lesions ($P=0.05$) (26).

Conclusion

Considering the importance of cervical cancer screening programs (36) based on primary health care and prevention system, the Pap smear test and the HPV genotyping are proposed to enhance the cervical cancer screening potential, but it seems that HPV genotyping has a significant financial expense and is not available for all regions. Our results suggest that Pap smear have the appropriate diagnostic accuracy in comparison with colposcopy and histopathology. Therefore, due to the efficacy of Pap smear test in combination with colposcopy and histopathology, and by considering the limitations in the health system to provide the HPV genotyping test, the importance of all these three tests should be considered.

Limitations

The main limitation of this study was its retrospective nature and the restrictions on HPV genotyping.

The strength of the study

Large sample size, duration of the study, and examination of cytology and histopathology samples by a skilled pathologists (to avoid inter observer biases), as well as conducting the study at a Obstetrics and Gynecology Academic Hospital with patients from lower or middle society classes.

Suggestions

Long-term prospective studies along with HPV genotyping test are recommended in order to improve the national guidelines in various regions.

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Conflict of Interest

The authors declared that there is no conflict of interest regarding the publication of this article.

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