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Comparison of Efficacy between Pap Smear and VIA as Cervical Cancer Screening

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Abstract

Cervical cancer is the second most common cancer among women worldwide. It typically has a long pre-invasive state. Therefore, cervical cancer screening, potentially could prevent the occurrence of invasive cervical carcinoma through detection and treatment of pre-malignant disease. Material and Methods: This study was concluded at Zahedan (Iran), in 2015 to 2016.Speculum examination was carried out in 100 women. All patients were screened by Pap smear and visual inspection with acetic acid 3%-5 % (VIA). Positive cases by both screening methods were subjected to colposcopy and biopsy. Results: 76 Out of 100 patients, were negative with both screening techniqes.18 patients were positive with visual inspection with acetic acid 3%-5 % (VIA). While Pap smear was positive in 12 subjects and 6 subjects were positive with both tests. Woman divided to age groups (<30 year, 30-50year and >50 year). Overall, the sensitivity of visual inspection with acetic acid 3%-5 % (VIA) and Pap smear were 94.11% and 41.17% respectively. Corresponding specificities were 97.59%and 93.97% for VIA and PAP smear respectively, positive predictive value (PPV) for visual inspection with acetic acid 3%-5%(VIA) 88.88%versus 58.32% for Pap smear, and negative predictive value (NPV) for visual inspection with acetic acid 3%-5% (VIA) was 98.78% versus 88.63% for pap smear. The accuracy of visual inspection with acetic acid 3%-5 % (VIA) was 97% compared to 85% of Pap smear. Conclusion: These results indicate that visual inspection with acetic acid 3%-5 %(VIA) is sensitive and specific in comparison with Pap smear. It could be valuable in detection of precancerous lesions especially in patients under 30 years old.

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Introduction

Cervical cancer is the second-most common gynecologic cancer among women in the world, with about 51,000 new cases each year, and mortality more than 288,000 people. 80% of cervical cancers occur in developing countries and it is the most common cause of mortality among middle-aged women in many developing countries (Comacho & Sellors, 2004)

Cervical cancer typically has premalignant period of a decade or more, and since the treatment of these pre-malignant lesions is effective, safe, and relatively inexpensive, (Feldman, 2014) if promptly diagnosed, premalignant lesions are almost completely preventable. The five-year survival rate is 90%. (Comacho & Sellors, 2004) Therefore, cervical cancer screening programs that detect prominent cellular changes as well as invasive and malignant changes in the cervix, can potentially prevent the onset of invasive cervical cancer through the diagnosis and treatment of pre-malignant. (Feldman, 2014)

Screening tests include the direct visual Inspection (DVI) of cervix and cytological methods, including Pap smear and DNA testing for high-risk human papillomavirus (HPV) types. (Sue et al., 2001)

Recently, some strategies have replaced Pap smear with simple eye screening techniques, including direct visual inspection (DVI), which cervix is visited after adding of 3-5% of acetic acid solution. These screening approaches are illustrated by large studies in limited facilities centers. (Sue et al., 2001)

In DVI screening, easy access to results is an important advantage and positive cases could be treated at the first visit (Feldman, 2014). Because of being of low cost, ease of use, and fast results, DVI will be useful screening test (Akinola et al., 2007). and reliable alternative to pap smears in limited facilities centers. (Tayyebet al., 2003) DVI is used to detect pre-malignant lesions

in cervical cancer, not only in centers with limited facilities, but also in health centers. (Jeronimo et al., 2005)

In a study by Sankaranarayanan and colleagues in India on 4444 women aged 30-59 years, they reported sensitivity of 88% and specificity of 78% for visual Inspection with Acetic Acid (VIA) and found that visual inspection with acetic acid 3%-5% reduces the incidence and mortality rate of cervical cancer (Sankaranarayana et al., 2007).

In a comparative study conducted in Sir Ganga Ram Hospital of Lahore (Pakistan) between January 1996 to December 1999, the visual inspection with acetic acid 3%-5%(VIA) method was compared with the Pap smear method. In this study 501 women were screened simultaneously with Pap smear and visual inspection with acetic acid 3%-5 % (VIA) with 3-5% Acetic Acid, both cases were followed up with colposcopy. The diagnostic accuracy of visual inspection with acetic acid 3%-5 % (VIA) was 77.5%, which showed a significant difference (P <0.01) compared with 52.8% of the Pap smear. These results indicate that visual inspection with acetic acid 3%-5 %(VIA) is more sensitive than pap smear and has more diagnostic accuracy in detecting pre-malignant lesions of the cervix. (Tayyebet al., 2003)

In a study by Abdel-Hady et al in Dakahlio Govenate in 2006, 5,000 women performed a visual inspection with acetic acid 3%-5%(VIA) test as cervical cancer screening, the susceptibility and negative predictive value of visual inspection with acetic acid 3%-5%(VIA) was 97%. The positive predictive value was 60% for all CIN grades and 90% for the High Grade CIN. They found that visual inspection with acetic acid 3%-5% (VIA), with relatively high false positive results, is an invaluable test for screening of cervical cancer. (Abdel-Hadi et al., 2006)

In a study by Shalakany and colleagues in Cairo, Egypt, 2049 women compared DVI as a primary method for detecting pre-malignant cervical lesions by cytological methods (pap smear) and found that DVI is a scientific method and has a high sensitivity Compared to cytological for diagnosis of the pre-malignant lesions of the cervix and can be used as a primary screening method in centers with limited facilities or undesirable cytological services. (El Shalaany et al., 2004)

The patients who refer to Ali ibn Abitalib hospital in Zahedan (Iran) mostly have low socioeconomic status, they are also low in public and cultural health, high parity and little knowledge about cancer screening, and then they have a high risk of cervical cancer. Most of the patients come from the districts area of the province and there is no possibility to go back to follow up. Because Pap smear screening is costly and difficult, and requires frequent visits, therefore, following up of the patients in most cases is not done correctly.

In this study, we determined to evaluate the diagnostic accuracy of the Pap smear method in screening of cervical cancer with DVI method that is a simple, reliable and fast method.

In the United States, cervical cancer is the sixth most common cancer in women after breast, lung, colon, endometrial and ovary carcinoma. (Scott et al., 2008) The average age of cancer diagnosis is 50 years old and the distribution chart has two peaks of age (35-39 years and 60-64 years). Worldwide, cervical cancer is still the leading cause of death among women due to cancer, with nearly 500,000 deaths a year. The lifetime risk of cervical cancer varies considerably from 0.4% in Israel to 3.5% in Cali in Colombi. (Scott et al., 2008).

Risk factors of cervical cancer including: Race, Reproductive and sexual factors, Smoking, Use of contraceptives, Immune suppression and HPV.

Over the past decade, epidemiological evidence has been collected suggesting that infection with human papillomavirus (HPV) is a possible etiologic factor in SCC (Squamous Cell Carcinoma) cervix. All known HPV types are similar in genomics and construction. They are uncoated viruses with a double-stranded DNA genome of 7800 to 7900 bp, and has a twenty-fold capsid. HPV DNA contains almost all cases (93%) of cervical cancer and its precursor lesions. While HIV infection seems to be a component of neoplastic deformity, it is unlikely to be fully adequate for this process.

Viral types that are high risk for cancer (including 56, 45, 31, 18, and 16) are commonly found in women with high-grade squamous intra epithelial lesions (HGSIL) and invasive cancer. HPV types 52, 51, 39, 35, 33 can be considered as having a moderate carcinogenic risk because they are associated with HGSIL, but are uncommonly found in an invasive carcinoma. (Scott et al., 2008; Harward et al., 2008).

Epidemiological case studies, often performed using HPV DNA techniques, have shown that extensive exposure to sexually activity of women and men has occurred with this virus, but most of the HPV-associated infections appear to be self-decreasing. . Koutsky and colleagues followed up young women whose evidence of the first contact with HPV, that was showed HPV reversed within 9-18 months of the first contact. The reason for the eradication of this viral infection is unknown, but the main theory in this regard is immune response to infection. (Scott et al., 2008)

The most common symptom of cervical cancer is bleeding or abnormal vaginal discharges. Abnormal bleeding may be post coital bleeding, intra menstrual, post menopause bleeding. If the bleeding is chronic, the patient may complain of fatigue or anemia symptoms. Yellow or serous vaginal discharge, often accompanied by bad odor, may accompany necrotizing or advanced carcinoma. Pelvic pain may be due to localized disease progression or tumor necrosis. Tumor development to the side walls of the pelvis may cause sciatic pain or low back pain associated with obstruction of the urinary tract or hydronephrosis. The metastasized tumor to the par aortic and iliac lymph nodes can develop into lumbosacral nerve roots, which is a symptom of lumbosacral pain. Urinary or rectal complaints (such as

hematuria, hematochezia, and fistula) can be associated with advanced invasive cervical carcinoma to the rectum or bladder. (Scott et al., 2008).

A cytological study of cervical and vaginal cells was initially proposed by Traut, Papa Nicolao in 1940 as a method for identifying cervical cancer and its precursors. Since then, cervical cytology is the most cost-effective and efficient way to screen of cancer. Screening for cervical cancer with Pap smear has reduced the incidence and mortality of cervical cancer in populations with Pap smear screening programs. A single Pap smear may reduce the risk of cervical cancer by 45%, and 9 negative smears reduce this risk by up to 99% during life. Cervical cancer screening methods including : (Scott et al., 2008)
1. Cervical cytology, 2. Liquid-based cytology, 3. HPV test, 4. Visual inspection with acetic acid3%-5% (VIA), 5. Colposcopy

Pap smear alone has only a sensitivity of about 60-50%, this means a test will not detect a cervical lesion in many women. Although the slow progress of CIN to an invasive cancer provides an opportunity for several cytological screenings over a period of a year. Also, even with limited sensitivity, if 3 consecutive tests are negative, less than 1% of the patient will have a high grade cervical lesions.Given the severe concerns about smear quality, the US government imposed requirements in 1988 to improve the status of clinical laboratories and the first Bethesda conference was held in 1990, and led to the invention of the Bethesda system. (Scott et al., 2008).

In the Bethesda system, the following groups are used, 1. Lack of evidence for malignant cells, 2. ASCUS (Atypical Squamous Cells of Undetermined Significance) 3. LSIL (low grade intraepitelial lesion).4.HSIL (high grade intraepitelial lesion) (Scott et al., 2008)

Visual inspection with acetic acid 3%-5 % (VIA) involves placing a vaginal speculum and applying of dilute acetic acid 3% to 5% with swabs on the cervix and viewing the cervix with naked eye. Normal squamous epithelium is pinkish and columnar epithelium is reddish. CIN lesions will change in white (acetowhite). The effect of acetic acid depends on the amount of non-transparent proteins and the presence of cytokeratin in the cervical epithelium, which increase in CIN. (1, 4).To reduce the false positive results rate, accurate training is needed. A high false positives with visual inspection with acetic acid 3%-5 %(VIA) can lead to an increase in treatment and unnecessary referrals of women. (Comacho & Sellors, 2004) Visual inspection with acetic acid 3%-5 %(VIA) may be less effective for women older than 60-50 years due to the tendency of the transitional area (TZ) (Comacho & Sellors, 2004). VIA results are considered as positive visual inspection with acetic acid 3%-5 %(VIA), negative and suspicious visual inspection with acetic acid 3%-5 %(VIA) for the cancer, negative visual inspection with acetic acid 3%-5 %(VIA) means there is no definite acetowhite lesion, positive result means the acetowhite regions, clearly distinct, clear, and sharp with or without margin are close to SCJ in TZ. (Akinola et al., 2007)

Findings that are suspected for cervical cancer include injured and proliferated lesions that may easily bleed. If there is any doubt about the description of the lesion and the result of the test, it can be repeated without causing bleeding. Positive visual inspection with acetic acid 3%-5 %(VIA) cases are referred for additional workup or treatment (Comacho & Sellors, 2004).

Material & Method

The study was a descriptive-analytic study of diagnostic type. The statistical population included women over 18 years who referred to the gynecology clinic of Ali Ibn Abi Talib Hospital in Zahedan (Iran) in 2011-2012. Exclusion criteria including: Individuals with total abdominal hysterectomy, virgin women, women who had been screened for less than 3 years, and patients who had a delivery during the 3 months ago , Curettage 1 month ago and obvious lesion. The test was also carried out in a condition where patients did not use vaginal cream for 72 hours prior to the test, and did not have an intercourse 24 hours prior to the test. Samples were selected using non-probabilistic sampling (successive and available samples). General information and demographic characteristics of the person including age, marriage age, and parity, number of partners, tobacco, and history of HPV, contraception, and results of Pap smear, visual inspection with acetic acid 3%-5% (VIA) test and biopsy and pathology tests were recorded in the information forms.

HPV accumulates in skin and mucosal epithelium and induces hyperplasia and leads to the formation of warts in the site of infection. Based on differences in DNA sequences, more than 70 different HPV types are identified, that 23 of them known to infect the reproductive system. Viruses that are less likely to be carcinogens include types 43, 42, 11, 6, 44, associated with condyloma acuminata and some types of low grade squamous intra epithelial lesions (LGSIL), but are rarely related to invasive cancer. (Scott et al., 2008) and a standard colposcopic assessment involves the accurate observation of the cervix with both white and green lights, after application of normal saline and acetic acid of 3-5%. lugol's iodine may also be used to color the cervix to detect areas of dysplasia, metaplasia or cylindrical epithelium. In order to evaluate the abnormally squamous epithelium, all squamous epithelium and the SCJ's place needs to be investigated (Comacho & Sellors, 2004)

In this survey, 100 women over the age of 18 years old were who referred to the gynecology clinic of Ali ibn Abi Talib hospital of Zahedan (Iran) in the year2011to2012 were studied. The women were selected using available samples and randomly. Then, the information form and informed consent were completed. In a completely private environment, the demographic data form was completed by the researcher. Female external genital system was examinated for lesions, papules, vesicles, ulcers, condiloma, discharge, redness, and swelling and inguinal lymph nodes by the expert gynecologist. The vaginal speculum was lubricated with warm water and gently and accurately placed into the vagina without damaging and the cervix was observed in terms of the presence of cervicitis, nabotian cysts, wounds, polyps,

leukoplakia, tumors, vesicles or cervical ulcers. The size and shape of the external cervical os were observed and were evaluated for signs of infection such as cervicitis, mucosal / peritoneal secretions. The approximate location of the cylindrical and squamous epithelium (SCJ) and deformation region (TZ) were detected, then, with spatula and swab , the samples from endocervical and exocervical was taken for Pap smear and fixed on the slide (using Pathofix fixator, manufactured by the antibacterial medicine company in Tehran) by the common gynecologist. Then, any mucus and secretion from the cervix were removed by cotton swab, and acetic acid 3% was rubbed by another swab ,at least 1 minute to wait until the acetic acid was absorbed , and then the results of the visual inspection with acetic acid 3%-5%(VIA) were visible. TZ, especially near SCJ, was carefully evaluated for any acetowhite and dense in the epithelium, and the internal TZ was observed for any white papules or acetowhite lesions, and the findings were noted, all of the procedures were performed by the expert gynecologist.

The lesions vary in size, thickness, opacity (white) and margin. Opaque lesions (whiter), thicker and larger, with a more specific margin near SCJ, showed more severe cervical disease. The findings were named on the presence or absence of acetowhite, respectively positive visual inspection with acetic acid 3%-5 % (VIA) or negative visual inspection with acetic acid 3%-5 % (VIA). The Pap smears were sent to the cytology lab and examined by experienced pathologist and the results were reported based on Bethesda's system.

The sample size was 100 people. Positive cases of both methods were referred to colposcopy and biopsy for diagnostic confirmation of the two tests, and the results of the biopsy were classified to positive and negative according to the presence or absence of dysplasia . The gold standard in this study was the result obtained from colposcopy, since it was difficult to obtain a biopsy from the whole population and was morally unacceptable, only the positive cases of each of the two screening tests were biopsied and the negative cases for both Pap test and visual inspection with acetic acid 3%-5%(VIA) were assumed negative.

Result

In this study, the population of women for the screening was between the ages of 18 and 75 years old, divided into 3 age groups under 30, 30-50, and over 50 years of age. From total of 100 women were studied , 26 women (26%) were under 30 years of age, 50 women (50%) aged 30-50, and 24 women (24%) were over the age of 50 years.

Out of 100 women studied, 18 had positive visual inspection with acetic acid 3%-5 % (VIA) and 12 had positive Pap smears. Of these, 6 patients were positive in both tests (Table 1) chi-square statistic is 9.46. The *p*-value is .002. The result is significant at $p < .05$.

In order to evaluate the degree of agreement between the two tests, Kappa coefficient was used to identify the positive cases. In this study, the degree of agreement (Kappa coefficient) of the Pap smear tests and visual inspection with acetic acid 3%-5 % (VIA) was 0.32. According to study of Landis and Koch (14), this degree of agreement in terms of classification is low.

20% of women in the age group of 30-50 years old, were positive visual inspection with acetic acid 3%-5%(VIA) , which was the same in the age group over 50 years. 12% of women under the age of 30 were positive for visual inspection with acetic acid 3%-5 %.

Of the total number of cases in the age group over 50 years old, 17% had positive pap smears that were the highest in comparison with those under the age of 30 years old (8%) and 30-50 (12%).

According to the above statistical results, most of the women who referring to Ali Ebne Abi Taleb hospital, were in the age range of 30 to 50 years old and positive visual inspection with acetic acid 3%-5%(VIA) cases were in the age group of 30-50 years and over 50 years old and positive Pap smears cases were in the age group over 50 years. This finding is somewhat consistent with the Danforth 2008 book, which lists the age distribution of cervical cancer in the age of 35-39 and 60-64 years old. Also, the marriage age of 74% of women , were under 20 years of age, and given the proven association between the low marriage age and the first sexual relationship with an increased risk of cervical cancer (Scott et al., 2008), higher rates of Pap smear and visual inspection with acetic acid 3%-5%(VIA) positive were in this age range.

Out of 18 positive visual inspection with acetic acid 3%-5%(VIA) women undergoing colposcopy and biopsy, 16 women (88.88%) were positive in biopsy , out of 12 positive Pap smears undergoing colposcopy and biopsy, 7 (58.33%) were positive biopsy results.

Given the main purpose of the study was to determine the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of each of the Pap test and visual inspection with acetic acid 3%-5%(VIA) tests based on age, the findings of each of the tests (table 2).

There are higher sensitivity of the visual inspection with acetic acid 3%-5 % (VIA) test compared to Pap smear, which is the same in all three age groups. This suggests that the Pap smear test is not helpful in identifying true positive patients as a screening test and cannot be a reliable test. Although the specifity of the two screening tests, are very close and approximately equal in the correct diagnosis of true negative patients. The positive predictive value of visual inspection with acetic acid 3%-5 %(VIA) was nearly double in comparison with Pap smear in all three age groups. That is, the ability of visual inspection with acetic acid 3%-5 %(VIA) in diagnosis ratio of the true positive patients per all of the positive results is high. The negative predictive value of the two tests is equal. The diagnostic accuracy of the visual inspection with acetic acid 3%-5 %(VIA) test or the

percentage of the correct responses, was higher in all three age groups than in the Pap smear. The visual inspection with acetic acid 3%-5 %(VIA) test generally has the highest diagnostic value in below the age of 30 years.

To investigate the possible relationship between the descriptive variables presented in the information form, it is worth noting that out of 17 positive cases in the biopsy (as a gold standard for the diagnosis of pre-malignant lesions of cervical cancer), 11 cases (64.7%) used OCP as contraception according to the Danforth 2008, this association was acceptable due to the effect of estrogen of the transformation zone (TZ).

4 patients (52.94%) of positive biopsy cases, had a history of cervicitis. As a result, according to Danforth book, 2008, cervicitis has identified as a risk factor for cervical cancer. Cervicitis can either be due to inflammation or as a result of dysplastic changes. (Scott et al., 2008). (Table 3) The chi-square statistic is 7.73. The *p*-value is .005. This result is significant at $p < .05$.

The range of marriage age was 10-32 years old, up to 63% of them were in the age range of 15-19 years old, and 82.35% of women of positive biopsy were in this age range, considering 74% of women were in the marriage age under 20 years old, and given the proven association between the low marriage age and the first sexual relationship with an increased risk of cervical cancer (Scott et al., 2008), the higher positive biopsy in this age range, is acceptable. (Table 4) The chi-square statistic is 11.00. The *p*-value is .004. The result is significant at $p < .05$.

None of the women studied had a history of genital warts based on information form.

Discussion

Pap smear screening (the common method of screening for cervical cancer in Iran) requires facilities, health care and trained people but in limited facilities centers is impossible to do Pap smear effectively. Recently, some strategies have replaced Pap smear with (VIA), the results of the research show that VIA is a cheap, accurate and simple test and is acceptable to the most women.

In this study, we compared the diagnostic accuracy of the Pap smear method with acetic anesthetic observation (VIA) for screening of cervical cancer. In our study, since it was difficult to obtain a biopsy from the whole population and was morally unacceptable, only the positive cases of each of the two screening tests were biopsied and the other cases in both method was assumed Negative biopsy. This research is consistent with the study conducted by Akinola et al., Which was done in Nigeria in 2007 for 186 women. (Akinola et al., 2007)

In this study, the population of women was between the ages of 18 and 75 years old, divided into 3 age groups under 30, 30-50, and over 50 years of age. Out of this number, 18 women had positive VIA and 12 had positive pap smears. Of these, 6 women were positive in both tests. It showed a low degree of agreement (0.32).

Most women were between the ages of 30 and 50 years. On the other hand, most cases of VIA were in the age group of 30-50 and over 50 years old but they were more than 50 years old in the pap smear. This conclusion is consistent with the Danfourth book2012.

The results of this study showed that visual inspection with acetic acid 3%-5% (VIA) in comparison with the pap smear has higher sensitivity, specificity, positive predictive value, and negative predictive value and diagnostic accuracy. In this study, visual inspection with acetic acid 3%-5%(VIA) had a 100% sensitivity in the age group of under 30 years old and 30-50 years old, which decreased by 80% in the age group above 50 years. In contrast, the sensitivity of Pap smear was 50% in the age group under 30 years of age, which did not change significantly with age.Totally and regardless of age groups, visual inspection with acetic acid 3%-5%(VIA) had final sensitivity of 94.11% versus sensitivity of 41.17% for Pap smear.

A study by Sankaranarayanan and colleagues reported a sensitivity of 88% for visual inspection with acetic acid 3%-5 % (VIA). In another study by Abdel-Hady in 2006, visual inspection with acetic acid 3%-5 %(VIA)'s sensitivity was 97%, that results almost was close to the results of visual inspection with acetic acid 3%-5 % (VIA) in this study. In a similar study in Pakistan, sensitivity was 93.9% for visual inspection with acetic acid 3%-5 %(VIA) and 46.9% for Pap smear. This study is consistent with our study. (Sankaranarayana et al., 2007).

A study by Akinola in 2007 found 100% sensitivity for visual inspection with acetic acid 3%-5 % (VIA) and 85.7% for Pap smear. The sensitivity of Pap smear in this study was reported higher than the sensitivity obtained in our study, as well as other similar articles. Which is probably due to the reduction of errors in sampling and interpretation (the two main problems of Pap smear in high false negative cases). (Akinola et al., 2007).

Most studies such as the present study agree on this topic , that Pap smear method is not sensitive and therefore has high false negative results, which causes problem in screening of cervical cancer, therefore, according to the above results, visual inspection with acetic acid 3%-5% (VIA) can be strongly considered as a sensitive test (even once tested) and valuable in screening of cervical cancer, and is a good alternative to successive pap smears, which it is currently, the gold standard of cervical cancer screening programs in most parts of the world including Iran.

In this study, visual inspection with acetic acid 3%-5% (VIA) had the most specificity in under 30 years old (100%), which decreased with age. In the age group of 30-50 years old and over 50 years old, it was 97.72% and 94.73%, respectively. Specificity of Pap smear were calculated in all three age groups and very close to the visual inspection with acetic acid 3%-5%

(VIA) , which did not change significantly with age (95%, 93.18% and 94.73% respectively).

Totally, regardless of age group, specifity of visual inspection with acetic acid 3%-5% (VIA) was 97.59% versus 93.97% for Pap smear.

In a comparative study conducted in Pakistan, specificity of Pap smears was 69.5% and visual inspection with acetic acid 3%-5%(VIA) 30.4%. That was very different from our study results. (Tayyebet al., 2003)

A study by Comacho in 2004 showed specificity of the visual inspection with acetic acid 3%-5%(VIA) in deprived areas is about 69%, and, specificity of the Pap smear was reported %98(Comacho & Sellors, 2004)
In another study by Doh in Cameroon in 2004, specificity of VIA was 77.6% versus 94.2% for Pap smear.(Doh et al., 2004) In the cross-sectional descriptive study conducted by Abdel-Hadi in India, it was 88.4% for visual inspection with acetic acid 3%-5 %(VIA) and 98.6% for Pap smear. The results of these studies were almost similar to the results of our study (specificity of visual inspection with acetic acid 3%-5% (VIA) and Pap smear are above 90%). (Abdel-Hadi et al., 2006)

Visual inspection with acetic acid 3%-5 %(VIA) in this study, the positive predictive value of VIA was higher in all three age groups and it is nearly twice as much as Pap smear. The positive predictive value of visual inspection with acetic acid 3%-5 %(VIA), as well as other evaluation variables, decreased with increasing of age. In contrast, Pap smear showed rising of positive predictive value with increasing age. This means that the ability of visual inspection with acetic acid 3%-5%(VIA) in diagnosing true positive among all positive cases was greater than Pap smear. In Pap smear, this result was higher in the age group over 50 years old (66.66%) than in other age groups (under30 years old and30-50 years old respectively 50%, and 57.14%. Totally without considering of age groups, the positive predictive value of visual inspection with acetic acid 3%-5%(VIA) was 88.88% versus 58.33% for the Pap smaer.In a study by Abdel-Hady in 2004, positive predictive value of visual inspection with acetic acid 3%-5% (VIA) reported59.7% (Abdel-Hadi et al., 2006). Another study by Akinola in 2007 found a positive predictive value of 20% for visual inspection with acetic acid 3%-5%(VIA)(4) .In a comparison study conducted by Doh in 2004, positive predictive value of Pap smear and visual inspection with acetic acid 3%-5%(VIA) were reported 67.2% and 44%, respectively (Doh et al., 2004).

According to the above studies, our results are consistent with none of the previous studies, and the results are completely different.The negative predictive value of visual inspection with acetic acid 3%-5%(VIA) was higher in all three age groups than the Pap smear, and the highest negative predictive value in the two methods (visual inspection with acetic acid 3%-5%(VIA) ,Pap smear)was under 30 years old.

Totally, regardless of age groups negative predictive value of visual inspection with acetic acid 3%-5 %(VIA) was 98.78% versus 88.63% for Pap smear.

In a study conducted by Abdel-Hady, negative predictive value of visual inspection with acetic acid 3%-5 %(VIA) was found 97%. (Abdel-Hadi et al., 2006)

In another study by Akinola, negative predictive value of visual inspection with acetic acid 3%-5 % (VIA) was reported 100%. (Akinola et al., 2007).

In a comparison study conducted by Doh, negative predictive value of visual inspection with acetic acid 3%-5 % (VIA) was, 91.3% and for Pap smear were reported 87.8%. The results of these studies were consistent with our study.(Doh et al., 2004)

The diagnostic accuracy of the visual inspection with acetic acid 3%-5 %(VIA) test for the age group under 30 years old was 100% that it decreased with increasing of the age. The diagnostic accuracy of Pap smear was observed in all three age groups below the visual inspection with acetic acid 3%-5 % (VIA).

In total, without regarding to age groups, the diagnostic accuracy of visual inspection with acetic acid 3%-5%(VIA) was 97% versus 85% for Pap smear.

In a comparative study conducted in Pakistan , diagnostic accuracy of visual inspection with acetic acid 3%-5% (VIA) was reported77.5% in comparison with 52.8% for pap Smear that because of low diagnostic accuracy of pap smear, this study was consistent with our study.

As a result, these findings suggest that the Pap smear method does not have the ability to identify the true positive as a screening test and it cannot be a reliable test (there are high false negative cases). Specificity of two screening tests, are very close and nearly equal in determining true negative. The positive predictive value of visual inspection with acetic acid 3%-5%(VIA) was nearly double in comparison with Pap smear in all three age groups,that is, the ability of visual inspection with acetic acid 3%-5%(VIA) in diagnosis of true positive cases is higher among all those who have positive results. The negative predictive value of the two method was close together. The diagnostic accuracy of the visual inspection with acetic acid 3%-5 % (VIA) was higher in all three age groups than the Pap smear.

Generally, the visual inspection with acetic acid 3%-5 %(VIA) has the highest diagnostic value in the age range below 30 years old.

According to the results, 64.7% of women with dysplastic changes in biopsy, had used OCP as a contraceptive method. This relationship is justified by the effect of estrogen and the availability of deformation region (TZ). The use of OCP is a proven risk factor in obstetric and maternal studies, including Danforth2008 (14).

Also, in this study, 74% of women had marriage age less than 20 years of age, which is an acceptable finding that show association between the low age of marriage and the first sexual relationship with an increased risk of cervical cancer in this age range. It is consistent with the results of other studies and findings in the books.

In this study, 52.94% of the positive biopsy cases, had a history of cervicitis. Cervicitis is reported as a risk factor for cervical cancer in the Women's and Midwifery Books, including Danfourth 2008 (Feldman, 2014).

Conclusion

These results indicate that visual inspection with acetic acid 3%-5 % (VIA) is more sensitive and specific and has a higher diagnostic accuracy than Pap smear. Therefore, it can be valuable in detecting the pre-malignant lesions of the cervical cancer, in order to reduce the incidence of cervical cancer and ultimately reducing of the mortality rate due to cancer. The results of this study, such as previous studies, show that being easy, low cost, and rapid results of visual inspection with acetic acid 3%-5% (VIA), as well as its high diagnostic accuracy of visual inspection with acetic acid 3%-5% (VIA) in comparison of Pap smear creates it as useful screening test in developing countries and areas with limited facilities, including Iran, especially in Sistan and Baluchistan province (IRAN).

Now that we have shown high sensitivity, specificity, and predictive value of visual inspection with acetic acid 3%-5 % (VIA) to reducing mortality rate of cervical cancer, we also found that visual inspection with acetic acid 3%-5 % (VIA) has a more acceptable outcome than Pap smear, then we made it a screening program. And in the first few years, cytology is used as a supporting and accompanying test. In a short period of time (1-2 weeks), nurses and midwives and other health care providers will be trained to conduct and interpret the test, and then even in small care centers during preconception care and gynecologic visits, they will be able to identify positive cases and refer them to the hospital for colposcopy.

Visual inspection with acetic acid 3%-5 % (VIA) does not require complicated equipment, it is low cost, and its results are immediately available, and the decision about the patient and, the treatment at the same visit is a special ability for it. Visual inspection with acetic acid 3%-5 %(VIA) can easily be accepted by developing countries including Iran, and even in developed countries. Of course, in some limited facilities, the possibility of replacing the visual inspection with acetic acid 3%-5%(VIA) is still under investigation, and more studies are needed to answer questions such as how to maximize visual inspection with acetic acid 3%-5%(VIA) testing and how quality of visual inspection with acetic acid 3%-5%(VIA) services can be guaranteed. And in what other way, visual inspection with acetic acid 3%-5 %(VIA) can enter cervical cancer screening programs.

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Table 1: Frequency of VIA and Pap smear in the population

		PAP		Total
		+	-	
VIA	Number + percent	6 % 33	12 % 67	18 % 100
	Number - Percent	6 % 7	76 % 93	82 % 100
Total	Number Percent	88 % 88	12 % 12	100 % 100

Chi-square statistic is 9.46. The *p*-value is .002. The result is significant at $p < .05$

Table 2: Evaluation variables of Pap smear and VIA tests in the population studied by age group

	Groups (Age)	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
VIA	<30 years old	% 100	% 100	% 100	% 100	% 100
	30-50 years old	% 100	% 97.72	% 90.90	% 100	% 98.14
	>50years old	% 80	% 94.73	% 80	% 94.73	% 91.66
PAP	<30 years old	% 50	% 95	% 50	% 90.47	% 86.36
	30-50 years old	% 40	% 93.18	% 57.14	% 82.23	% 83.33
	>50years old	% 50	94.73	% 66.66	% 90	% 86.95

Table 3: relationship between cervicitis and dysplasia

		Cervicitis		Total
		+	_	
Biopsy	Number + Percent	9 % 52.94	8 % 47.05	17 % 100
	Number - Percent	17 % 20.48	66 % 79.51	83 % 100
Total	Number Percent	26 % 26	74 % 74	100 % 100

The chi-square statistic is 7.73. The *p*-value is .005. This result is significant at $p < .05$.

Table 4: Relationship between marriage age and dysplasia

			Marriage age range			Total
			10-14	15-19	>20	
Biopsy	+	Number Percent	2 % 11.76	14 % 82.35	1 % 5.88	17 % 17
	-	Number percent	26 % 31.32	31 % 37.34	26 31.32%	83 % 100
Total	Number percent		28 % 28	46 % 46	26 26%	100 % 100

The chi-square statistic is 11.00. The *p*-value is .004. The result is significant at $p < .05$.