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Evaluating sociodemographic factors influencing cervical cancer and detection of cervical lesion by screening methods; visual inspection with acetic acid (VIA) and Papanicolaou (Pap) smear among Pakistani women

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Abstract

Cervical cancer is the most prevalent gynecological malignancy in low to middle-income countries. In Pakistan, cervical cancer ranks as the 3rd leading cause of death in females. The important reason for this higher mortality rate is lack of valuable screening programs. Cancer of the cervix is a preventable disease. The purpose of this study was to determine the socio-demographic factors influencing cervical cancer screening and to assess the role of screening test for early detection of cervical carcinoma in the Pakistani female. Between, January 2013 to December 2014 cervical smears were taken from married females with gynecological problems visiting Pakistan Institute of Medical sciences. Pap smears were also obtained from Armed forces institute of Pathology, Rawalpindi. In the present study, a total of 118 cervical smears were screened using Pap smear test. All patients were also subjected to VIA. The mean age of the female patients was 35.78 ± 9.8 years. There were 42(35.5%) normal Pap smear, 33(27.9%) inflammatory, 11(9.3%) LSIL, 5(4.2%) HSIL and 18(15.2%) abnormal Pap smear. Acetic acid (VIA) was positive in 27/118 (22.8%) patients. Early Pap smear test can be effective in diagnosis of premalignant lesions of cervix. However, visual inspection of the cervix with acetic acid is an effective method for immediate detection of cervical malignancies in low resource country like Pakistan. Nationwide programs should be established to increase knowledge of cervical cancer and its screening to decrease late presentation and rate of mortality.

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Introduction

Cancer is a class of disease in which there is continual unregulated proliferation of abnormal cells in the body. Cancer cells have potential to metastasize adjacent normal tissues, organs and eventually spread throughout the body. There are 277 distinct types of cancer. The most noteworthy types of cancer in males occur in the lungs, urinary bladder, colon rectum and prostate respectively. Breast, lungs, thyroid, cervical and uterus are commonly occurring cancer in females. Blood cancer is the most prevalent cancer that affects children (Siegel *et al.,* 2014; Topcul and Cetin 2014).

Cervical cancer develops in the cell lining of the cervix in a female genital tract. There are pathologically distinct types of cervical cancer characterized by their location in the cervix. These are squamous cell carcinoma (cancer of ectocervix), adenocarcinoma (cancer of endocervix) and adenosquamous carcinoma(Stumbar *et al.,* 2019).

Oncogenic human papillomavirus infection has been recognized as the major etiologic agent of cervical cancer. Individuals infected with human papillomavirus have an asymptomatic course, 90% of clearance of virus occurs within 1 or 2 years. However, the remaining 10% will advance to a persistent infection that has increased risk in developing cervical carcinoma. Of these 10%, about one-half will develop malignancy by year 30 of persistent high-risk HPV infection. Many established risk factors associated with progression from human papillomavirus infection to invasive cancer include early onset of sexual activity, multiple sex partners, smoking and use of oral contraceptives (De Villiers *et al.,* 2004; Oh *et al.,* 2016).

A pre-malignant state of the cervix (Cervical intra epithelial neoplasia) is usually asymptomatic and it can be identified by routine cytological screening tests. Incidence of cervical cancer has reduced subsequently by the introduction of Papanicolaou (abbreviated as Pap) smear test in the mid-20th century. It detects any malignancy in the cervix at its early stage. Visual screening of the cervix by means of acetic acid has efficiently used in early detection. VIA (visual inspection with acetic acid) is a simple and inexpensive test in low resource setup (Bora *et al.,* 2017).

Globally, cervical carcinoma is the leading cause of gynecologic cancer related deaths. There is a significantly greater difference in terms of cervical cancer incidence among low to middle-income countries and high-income countries. This distinction is presumably due to introduction of efficient screening through Papanicolaou (Pap) smear, primary preventions and vaccination programs in the developed countries (Wentzensen *et al.,* 2017; Oyervides-Munoz *et al.,* 2018; Vu *et al.,* 2018). Cancer of the cervix can be preventable, an early detection plays vital role in diagnosis and disease management (Naz *et al.,* 2018). In developing nations 85% of gynecological malignancies are incurable because of their disclosure at advanced stage(Zhao *et al.,* 2012). Asian countries contribute to half of the global burden of cervical cancer cases annually (Garland *et al.,* 2012). The high incidence in Asia is due to lack of awareness in regard to human papillomavirus infection, screening and vaccination programs (Daniyal *et al.,* 2015).

Islamic Republic of Pakistan is a developing country and cervical cancer is a major public health threat because of the late-stage presentation of disease. The higher mortality rate is due to absence of valuable cancer screening curriculums and vaccination programs nationwide. Social and religious taboos and stigma associated with the sexually transmitted nature of HPV infection possibly a significant barrier in study of disease epidemiology. As a result there has been lack of documentation concerning the incidence of cervical cancer in the country (Gul *et al.,* 2015; Aziz *et al.,* 2018). This study aimed to assess cervical cancer screening aspects in Pakistani women via Pap smear and visual inspection with acetic acid (VIA). In addition, the relationship between cervical cancer screening and the social and demographic characteristics was also evaluated.

Material and methods

Sample collection

A descriptive cross-sectional study was conducted at Department of Virology and Department of Histopathology in National Institute of Health (NIH), Islamabad, since January 2013 till December 2014, after the approval of the study protocol by the Ethical Review Committee of NIH and Quaid-i- Azam University, Islamabad. The study population consisted of women attending Outpatient Department of Gynae/Obstetrics in Pakistan Institute of Medical Sciences (PIMS), Islamabad and samples were also obtained from Armed Forces Institute of Pathology Rawalpindi (AFIP). PIMS and AFIP are major health institutes of Pakistan with an ethnic diverse patient population. A written consent was obtained from female patients before doing the procedure. Patients were also informed about the importance of screening tests and its benefits and associated risk factors.

Inclusion and exclusion Criteria

In this study, 250 sexually active women of age group 21–60 years old were recruited to the study but only 118 cases were included. The inclusion criteria are being Pakistan, married women, abnormal vaginal discharge, clinically suspicious looking cervix and no previous gynecological malignancy diagnosis. Women presenting with any or all of following: vaginal bleeding, pregnancy, ongoing menstruation, history of cervical abnormalities, amputated cervix, previous total hysterectomy, using immunosuppressant were excluded from study.

Data collection for sociodemographic features

Firstly, general history of all eligible females were taken in a special data entry sheet, which was consisted of two parts: first part includes social demographic information: age, marital status education, parity and socio economic status and the second part comprised of local pelvic examination: vagina and cervix.

Pelvic Examination

Firstly, examination of vulva for any abnormalities, infection wart was documented. A direct visual inspection of the vagina and cervix was performed to observe any visible abrasion by inserting Cusco's bivalve vaginal speculum in the lithotomy position. Any mucus or vaginal discharge was removed by using cotton gauzes.

Secondly, a Pap smear was taken by gentle scrapping of the squamocolumner junction throughout the circumference by the help of Ayre's spatula. The material on spatula was transferred on glass slide and a smear was prepared, immediately fixed in 95% alcohol and later stained by Papanicolaou stain method. The Pap smear test was reported by the Bethesda system. There are four categories: atypical squamous cell of undetermined significance (ASCUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCC). Any slide with dysplasia (mild, moderate, severe), carcinoma in situ (CIS) or squamous cell carcinoma were considered positive histopathologically.

Thirdly, Visual inspection with acetic acid (VIA) was performed by a cotton swab soaked in freshly prepared 5% acetic acid solution and applied for 1 minute on cervix. A well-defined opaque aceto-white lesion next or close to the squamocolumner junction indicates positive VIA result. All Pap slides were reviewed by histopathologists in PIMS, AFIP and NIH and reported according to Bethesda system.

Data analysis

Data was analyzed by using IBM SPSS statistics 21. Descriptive statistics were applied for data analysis. Means and standard deviations were calculated for age and frequencies were calculated for all qualitative variables in present study.

Results

Sociodemographic features

250 married Pakistani females with gynecological problems included in the present study. 132 females who did not fit in to the inclusion criteria were excluded. Total 118 females were considered relevant for the screening study. Mostly females belong to

rural areas 68(57.62%) while 50(42.37%) belong to urban areas. Among 118 female patients 52(44%) were Punjabi, 7(5.9%) Brusho, 7(5.9%) Sariki, 31(26.3%) Pashtuns, 18(15.3%) had Kashmiri ethnicity. The mean age of the female patients in current study was 35.78 ± 9.8 years. Among the 118 patients were 104 married, 11 divorced while 3 widow. Mean age at marriage was 21.77± 4.8 years and mean marital duration was 14.01 ± 10.87 year. Moreover, mean age at first pregnancy was 18.06 ±9.77 years old. Out of 118 females 33 (27.9%) were nulliparous while 85(72%) were parous. Only 40(33.9%) female patients documented use of contraceptives methods. Majority of participants had low income 69(58.5%), only few had high income 17(14.4%) while the rest had middle income 32(27.1%) to live on. Social demographic characteristics of females who participated in the study are detailed in Table 1.

Table 1. Social Demographic characteristics of the females who participated in screening study.

Socio-demographic characteristics	Number (%)
Marital status	
Married	104(88.1%)
Divorce	11(9.3%)
Widow	3(2.5%)
Area	
Rural	68(57.62%)
Urban	50(42.37%)
Ethnicity	
Punjabi	52(44.%)
Brusho	7(5.9%)
Sariki	7(5.9%)
Pashtuns	31(26.3%)
Kashmiri	18(15.3%)
Other	3(2.5%)
Socio economic status	
Low	69(58.5%)
Middle	32(27.1%)
High	17(14.4%)
Age at marriage (years)	
≤ 20	69(58.5%)
21-30	35(29.7%)
30-40	14(11.9%)
Duration of marriage(years)	
>5	30(25.4%)
5-10	35(29.7%)
11-20	26(22.0%)
>20	27(22.9%)
Age at first pregnancy (years)	
≤ 20	63(53.4%)
21-30	45(38.1%)
>30	10(8.5%)
Parity	
None	33 (27.9%)
1	20(16.9%)
2or 3	37(31.3%)
More than 3	28(23.7%)
Contraception	
None	78(66.1%)
Yes	40(33.9%)

66 (55%) female patients had education (higher/secondary/ primary) while 52(44%) were illiterate. 35(29.7%) patient's husband had never been to school, 13(11%) had primary, 15(12.7%) secondary education while 16(13.6%) were postgraduate. Detailed education status of husband and wife is shown in Table 2. Majority of females 84(71.1%) included in the study were unemployed while 99(83.8%) of patient's husband were employed. None of them gave history of STI (sexually transmitted infection). Most of the female patients gave history of smoking of husband 78(66%) while 7(5%) had stopped smoking. Among 118 females, 114(96.6%) never smoked. Moreover, 115 females were in monogamous relationship as mentioned in table 2.

Table 2. Knowledge about age, education and employment of the females and their respective husbands.

Age (years)	Female patient (%)	Patient husband (%)
<20	0	12(10.2)
21-30	47(39.8%)	18(15.3)
31-40	41(34.7%)	47(39.8%)
41-50	22(18.6%)	34(28.8%)
>50	8(6.8%)	7(5.9%)
Education		
Illiterate	52(44.1%)	35(29.7%)
Primary	22(18.6)	13(11%)
Secondary	15(12.7)	15(12.7%)
Higher secondary	11(9.3%)	18(15.3%)
Graduate	12(10.2%)	12(17.8%)
Post Graduate	6(5.1%)	16(13.6%)
Employment status		
Unemployed	84(71.1%)	19 (16.1%)
Employed	34 (28.8%)	99 (83.8%)
smoking		
Yes	4(3.4%)	78(66%)
Never	114(96.6%)	33(28%)
Stopped	0	7(5%)
No. of marriages		
1	115	91(77.11%)
>1	3	27(22.88%)
History of STI	No	No

Pelvic examination, Pap and VIA findings

Vaginal discharge is the most frequent presenting complaint 90 (76%) followed by lower abdominal pain 11(9.3%) and back pain 5(4.2%). Eight females (6.7%) had gynecological complaint of itchiness as mentioned in table 3. Vaginal speculum examination findings showed 54(45.76%) normal cervix, 26(22.03%) suspicious cervix and 38(32.20%) chronic cervicitis respectively. 42(35.5%) Pap smears were reported normal, 33(27.9%) were inflammatory while 18(15.2%) were reported as abnormal pap smear. 11(9.3%) Pap smear was documented as LSIL, 5(4.2%) as HSIL and 9(7.6%) reported as atypical cells (table 4).

Acetic acid (VIA) was positive in 27/118 (22.8%) patients and negative for 91(77.2%) as shown in table 5.

Table 3. Common gynecological complaints of female patient.

Clinical complaint	Number (%)
Vaginal discharge	90(76%)
Lower abdominal pain	11(9.3%)
Back pain	5(4.2%)
Itchiness	8(6.7%)
Painful intercourse	4(3.3%)

Age distribution of the 118 patients with positive VIA and Pap smear is shown in Table 6. Of the 27 females with positive VIA, 9 were between 31-40 years, 12 females were between 41-50 years and further 6 females have age greater than 50.

Table 4. Pap smear findings of present study.

Pap smear	Number (%)
Normal	42(35.5%)
Inflammatory	33(27.9%)
Abnormal pap smear	18(15.2%)
LSIL	11(9.3%)
HSIL	5(4.2%)
Atypical cells	9(7.6%)

Out of 16 positive Pap smear, 7 females were between 31-40 years and 8 females were between 41-50 years respectively.

Discussion

Cervical carcinoma influences females in their reproductive years. Carcinogenic transformation of HPV infection to intrusive malignancy is a very long process and it gives adequate chances to detect the stage of disease, its diagnoses and treatment. Therefore, cytological screening is a major secondary prevention approach for early detection(Basu *et al.,* 2018; Kadam *et al.,* 2018).

In low-middle income countries low coverage of screening facilities for cervical cancer has been ascribed to personal and structural barricades. Personal barricades comprises of less information concerning cervical malignancy, screening practices, preventions and acumens to socio-religious convictions. A structural barricade involves inaccessibility of screening programs, inadequate resources (material and financial) and poor health-care services (Denny *et al.,* 2006; Morema *et al.,* 2014; Finocchario-Kessler *et al.,* 2016).

This study focused on assessing cervical cancer screening aspects in Pakistani women and evaluated the relationship between cervical cancer screening and the social and demographic characteristics. Numerous studies proposed that knowledge regarding cervical carcinoma and Pap smear test are influenced by sociodemographic factors such as age, education, husband's education, parity and household income (Al-Shaikh *et al.,* 2014; Mulhim *et al.,* 2014; Du *et al.,* 2015; Strohl *et al.,* 2015).

All female patients in the present study were married and the mean age is 35.78 ± 9.8 years. Many studies have documented that the average age of female to develop cancer of cervix lies between 40-50 years old. However, its precursor lesion develops earlier (5-10 years)(Saraiya *et al.,* 2013; Shanmugham *et al.,* 2014; Maleki *et al.,* 2015). Hence, the present study also highlights that married females should have one screening test at age of 35years old as this cervical

cancer screening play a key role in diagnosis and disease management.

In present study, mean age at first pregnancy was 18.06 ±9.77 years old. Previous data showed that birth of child at very early age could influence the risk of cervix carcinogenesis. This susceptibility may be due to steroidal hormone influence on human papillomavirus infection, host immune response to HPV infection in puberty and biological immaturity in the course of adolescence (Elson *et al.,* 2000; Louie *et al.,* 2009).

Table 5. Visual inspection with acetic acid findings.

VIA	Number (%)
Positive	27 (22.8%)
Negative	91(77.2%)

The present study also assessed the influence of some significant independent variables like; education, qualification and employment status of husband, family income, area, parity, smoking on cervical cancer screening. In our study most of the patients are from Rural areas 68(57.62%) belong to low (58.5%) income socio economic status. The study found in agreement with other local and international studies that poor socioeconomic status and lack of education, smoking poor hygiene has positive association with progression of disease (Ali *et al.,* 2010; Das *et al.,* 2013; Jbeen *et al.,* 2013).

Hence, higher level of education is positively associated with better knowledge about cervical cancer screening (Aldohaian *et al.,* 2019).

Table 6. Age distribution of the 118 patients with positive VIA and pap smear.

Age (years)	Total no. of patients	Positive VIA (Total=27)	Positive pap smear (Total=16)
21-30	47	0	0
31-40	41	9	7
41-50	22	12	8
>50	8	6	1

Vaginal discharge is a very common gynecological complaint. The present study showed that 90(76%) female patients have clinical complaint of vaginal discharge. This validated with the findings of various global investigations (Samanta *et al.,* 2011; Yasmin and Mukherjee 2012; Salih *et al.,* 2017).

This study revealed that 118 of female patient had undergone a Pap test. Among them dysplastic changes were observed in 16, in which (11 (9.3%) showed low grade squamous intraepithelial lesion and 5(4.2%) patients have high grade squamous intraepithelial lesion. Several local studies have documented a relation between cervical malignancy and abnormal cells in cervix detected on Pap smear (Khattak *et al.,* 2006; Haider *et al.,* 2013; Khan Inamullah *et al.,* 2013).

The rate of detection of cervical dysplasia in VIA is 22.8 % in our study. Numerous studies had documented 1.7 % to 29% positive VIA cases (Tayyeb *et al.,* 2003; Bomfim *et al.,* 2005; Albert *et al.,* 2012). This variability in rate is because of various criteria utilized in different investigations because of absence of standard measures for positive outcomes.

Our finding in the present study is the VIA highest positivity rate is in the age group of 40-50years. Results of the present study are similar with other studies that VIA and Pap smear positivity frequency increases with the age (Gravitt *et al.,* 2010; Arun *et al.,* 2018).

Pakistan is an Islamic state, it assimilate religion in all areas of life including law, culture and society. But

prevalence of a large number of myths, socio-cultural and religious taboos has adversely affected the cervical cancer screening (Shafiq and Ali 2006; Khan Saeed *et al.,* 2007).

False elucidation of Islamic convictions prompted 42% of females to assume that "if cervical cancer is a piece of my fate, having a screening test can't forestall it". Islam urges muslims to perform self-care and seek out treatment.

It was narrated that the Holy Prophet Hazrat Muhammad (peace be upon him) said: “Seek treatment, O slaves of Allah! For Allah does not create any disease but he also creates with it the cure, except for old age.”(Salman 2012; Aldohaian *et al.* 2019).

Several studies suggested the role of self-sampling technique as many women may incline toward a test that can be performed in privacy by the woman herself in her home to avoid discomfort or embracement with in the medical staff (Martin 2000; Gok *et al.,* 2010; Singla and Komesaroff 2018).

Numerous studies recommended that media should play its key role in disseminating information and awareness about cervical cancer and importance of Pap smear test (Cetisli *et al.,* 2016; Aldohaian *et al.* 2019).

Conclusion

Despite the fact that the frequency of cervix carcinoma in Pakistan is lower than other western nations, however death rate is high because of lack of awareness regarding cervical screening, inaccessibility of Pap smear test and late presentation of cervical malignancies. Diagnosis of cervical cancer at late stage needs implementations of cervical cancer screening programs to decrease burden of disease.

The present study emphasizes on establishment of early diagnostic camps and public health education programs to hold time to time on national level to upgrade awareness and guidance to save the lives of females in Pakistan.

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