

## RESEARCH ARTICLE

# Factors Associated with Delayed Diagnosis of Cervical Cancer in Iran - a Survey in Isfahan City

Fariba Behnamfar, Mahboobeh Azadehrah\*

### Abstract

**Background:** In the absence of routine screening program for cervical cancer in Iran and high rate of diagnosed cancer in its advanced stage, recognition of sociodemographic factors related to delayed diagnosis of cancer in Iran could be helpful in reducing the burden of disease in our community. The aim of this study was to determine the stage of cervical cancer at diagnosis and factors related to delayed diagnosis of cervical cancer in Isfahan, Iran. **Materials and Methods:** In this cross sectional study women diagnosed with cervical cancer for the first time by histo-pathological examination were enrolled. According to the clinical and paraclinical findings and staging of the cancer, they were classified into early and delayed diagnosis of cervical cancer. Sociodemographic factors were compared in the two groups. **Results:** In this study of 55 women mean age was  $48.3 \pm 12.0$ . According to our classification 6/55 (10.9%) and 49/55 (89.1%) of them had early and delayed diagnosis of cervical cancer. Delayed diagnosis of the cancer was significantly higher in patients with lower degree of education, lower socioeconomic status, having smoker and addict husband and those who did not have a history of Pap smear test ( $p < 0.05$ ). **Conclusions:** The results of this study indicated risk factors related to delayed diagnosis of cervical cancer. The affected women should be targeted for implementation of specialized educational programmes for improving knowledge and screening test.

**Keywords:** Cervical cancer - pap smear - diagnosis - delay - Isfahan, Iran

*Asian Pac J Cancer Prev*, **16** (2), 635-639

### Introduction

Cervical cancer with an estimated 529,800 new cases worldwide is considered as one of the most common cancer among women worldwide. It constitutes approximately 8% of the global burden of cancer among women (Ferlay et al., 2010; Arbyn et al., 2011). More than 85% of the cases have reported in developing countries (Jemal et al., 2011).

The estimated age-standardized incidence rate (ASR) of cervical cancer in Iran have reported to be 2.5 per 100,000 in pathology-based cancer registries and the mortality to incidence ratio was 42% according to a recent study in Iran (Khorasanizadeh et al., 2013).

Cervical cancer is a curable and preventable disease if it diagnosed in the early stage of malignancy i.e at the precancerous stage (Devi et al., 2007). Whereas advanced stage of the disease has poor prognosis and is correlated with lower survival rates. Advanced cervical cancer is one of the major causes of cancer related mortality in women specially in low- and medium-income countries mostly due to poor access to appropriate management (Vinh-Hung et al., 2007; Thomson and Forman, 2009).

Recently the concept of delayed diagnosis has become as an important issue in the cancer prevention and

treatment. The concept is categorized in four components including patient delay, health care provider delay, referral delay and system delay. Though all of the mentioned delays have important role in the prevention, diagnosis and management of the disease but it seems that in our country and other developing countries patients and health care providers delay have more crucial role (Hansen et al., 2008; Berraho et al., 2012; Gyenwali et al., 2014).

Several studies worldwide have investigated the factors associated with delayed diagnosis of the cancer and disparities in its mortality rate in different racial, geographic and socio-economic groups (Allgar et al., 2005; Brewer et al., 2005; Yu et al., 2005; Ibfelt et al., 2012). However knowledge of delays for this cancer could be useful in establishing comprehensive preventative strategies.

Though the incidence rate of cervical cancer is low in Iran (Arbyn et al., 2011) but the mortality to incidence ratio is high which indicates that most of the cancer cases are diagnosed in advanced stages. Factors such as unavailability to routine screening, inadequate follow-up of abnormal Pap smears and possibly low awareness of women's population regarding the course of the disease could explain the higher mortality of the cancer in our community (Khorasanizadeh et al., 2013). So, in the

absence of routine screening program for cervical cancer in Iran and high rate of diagnosed cancer in its advanced stage, recognition of socio-demographic factors related to delayed diagnosis of cancer in Iran could be helpful in eliminating the burden of disease in our community. The aim of this study is to determine factors related to delayed diagnosis of cervical cancer in Isfahan, Iran.

## Materials and Methods

This study designed as cross sectional study with qualitative approach. In this study women aged 30-60 years diagnosed with cervical cancer for the first time by histo-pathological examination of cervix referred to three obstetrics and gynecology specialized cancer clinics in three hospitals of Isfahan during March 2013-March 2014 were enrolled.

The protocol of study was approved by Regional Bioethics Committee of Isfahan University of Medical Sciences. Written informed consent was obtained from all selected patients.

Inclusion criteria were all women who diagnosed with cervical cancer based on histopathological examination of cervix (conization or biopsy). Women with diagnosed cancer other than cervical cancer were excluded.

All selected patients recalled and their medical files from mentioned three clinics was referred to the oncology clinics of Shahid Beheshti hospital for more investigation. Written informed consent was obtained from all participants after describing the aim and details of the method of the study.

Recalled patients examined clinically by gynecologist (MA). A complete pelvic and lymph nodes (axillary, supraclavicular, inguinal, femoral) examination was performed by the gynecologist in order to determine the metastatic cases. The stage of cervical cancer at diagnosis was defined according to International Federation of Gynecology and Obstetrics (FIGO) system of staging of gynecological cancer (Benedet et al., 2000). Chest X-ray was done in all studied patients. Other complementary radiological tests were done according to the condition of the patients. If patients had a history of participating in cervical cancer screening program, if their histopathologic smears were available, they reviewed once more. According to the clinical and paraclinical findings the stage of cancer was determined in each patient. Basis of the stage of the cervical cancer at diagnosis, stage IA-1 were defined as early diagnosis and stage IA-2 and above were considered as late or delayed diagnosis. During the patients visit and after clinical examination, they interviewed by trained

**Table 1. Demographic Factors and Cancer Related Factors in Women with Early and Delayed Diagnosis of Cervical Cancer in Isfahan, Iran**

Variables		Women with early diagnosis of cervical cancer n=6	Women with delayed diagnosis of cervical cancer n=49	p value
Age of marriage(years)		17.16±3.37	16.08±4.36	>0.05
Frequency of marriage in patients		1.16 0.40	1.12 0.33	>0.05
Frequency of marriage in husband		1.0 0.0	1.12 0.33	>0.05
Parity		4.5 2.50	4.76 2.46	>0.05
Gravity		3.0 1.26	4.32 2.40	>0.05
Education of patient	Illiterate	0	15 (30.63)	
	Elementary-diploma	4 (66.7)	24 (48.97)	<0.001
	Higher than diploma	2 (33.3)	10 (20.40)	
Education of husband	Illiterate	1 (16.7)	16 (32.65)	
	Elementary-diploma	3 (50)	25 (51.02)	>0.05
	Higher than diploma	2 (33.3)	8 (16.32)	
Smoking	Patients	0 (0%)	3 (6.12%)	>0.05
	Husbands	1 (16.7%)	32 (65.3%)	<0.001
Addiction	Patients	0 (0%)	3 (6.12%)	>0.05
	Husbands	1 (16.7%)	21 (42.85%)	<0.001
Place of residence	Urban	6 (100)	37 (75.52)	>0.05
	Rural	0 (0)	12 (24.48)	
Socioeconomic condition	Low	3 (50)	3 (6.12)	
	Moderate	3 (50)	8 (16.32)	<0.001
	High	0 (0)	38 (77.56)	
Health insurance	Non	1 (16.7)	4 (8.16)	
	Rural	0 (0)	9 (18.36)	>0.05
	others	5 (83.3)	36 (73.46)	
History of pap smear	Never	2 (33.3)	28 (57.14)	
	During last 3 years	2 (33.3)	14 (28.57)	<0.001
	More than 3 years age	2 (33.3)	7 (14.29)	
Signs	Abnormal pap smear	4 (66.6)	0 (0)	
	Abnormal vaginal bleeding	0	28 (57.14)	
	Post-menopausal bleeding	1 (16.7)	12 (24.48)	>0.05
	Discharge	1 (16.7)	10 (20.40)	
Histopathology	Squamous cell carcinoma	6	41 (83.67)	>0.05
	Adenocarcinoma	0	7 (14.28)	
	Adenosquamous carcinoma	0	1 (2.04)	

nurses for following information; age, marital status (age of marriage and frequency), degree of education (no education, elementary/diploma, high education), smoking (patient and her husband), addiction (and her husband), socioeconomic status, insurance status, place of residence (urban or rural), hepatitis B infection, first symptom of the disease (abnormal pop smear, vaginal bleeding, vaginal discharge, pain and etc.), obstetrics history (parity and etc.). Mentioned variables were compared in patients with early and late diagnosis.

#### *Statistical analysis*

Data analyzed using SPSS ver. 18 (SPSS Inc., Chicago, Ill., USA). Quantitative and qualitative variables in two studied groups was compared using t-test and chi-square tests.

## **Results**

In this study 55 women with cervical cancer enrolled. Mean age of studied population was  $48.26 \pm 12.01$ . According to our classification 6/55 (10.9%) and 49/55 (89.1%) of them had early and delayed diagnosis of cervical cancer. Distributions of different pathologies of cervical cancers were as follows; Squamous cell carcinoma; 48 (85.71%), adenocarcinoma; 7 (12.5%) and adenosquamous carcinoma; 1 (1.79%). Demographic factors and cancer related factors in two studied groups are presented in Table 1. There were not any cases of hepatitis B infection.

## **Discussion**

In this study we evaluated different socio demographic factors associated with delay diagnosis of cervical cancer among patients diagnosed with the disease in Isfahan. Patients with lower degree of education, lower socioeconomic status, having smoker and addict husband as well as those who did not history of pop smear test had higher probability for delayed diagnosis of cervical cancer.

The rate of delayed diagnosis in this study was high (89.09%). The rate was higher than that reported in Sudan (72%) (Ibrahim et al., 2011) and Nepal (80.9%) (Gyenwali et al., 2013). The rate indicated that though the overall prevalence of the cancer was not high in our population but higher occurrence of advanced stage cervical cancers in our community emphasized on the necessity of general screening program or improvement of population awareness in this regard.

As mentioned, absence of nationwide screening program in communities such as Iran led us to plan other multi factorial interventional studies to provide more proper preventative strategies for reduce both patients and health care professionals delay. The goal could be achieved if its associated risk factors identified. Some previous studies have investigated risk factors related to delay diagnosis of cervical cancer. Reported results regarding the role of different factors were not similar in different studies. It may be due to differences in the methods of studies, ethnicity, environmental and socioeconomic factors of the populations.

Gyenwali et al. (2013) in Nepal determined the factors associated with late diagnosis of cervical cancer among 110 patients with cervical cancer. They indicated that higher education and having symptoms of the disease specially abnormal vaginal bleeding as early symptom are related to lower delayed diagnosis of the cancer.

Tanturovski et al. (2013) have investigated the association between certain socio-demographic factors and delayed diagnosis of invasive cervical cancer. Their studied population consists of 115 patients. Their results indicated that delayed presentation of the cancer is associated with lower degree of education, low monthly income, had no family history of invasive cervical cancer in first degree female relatives and poor genital hygiene.

Ibrahim et al. (2011) in Sudan have studied predictors of cervical cancer in its advanced stage. They showed that, delayed diagnosis of the disease is associated with older age, ethnicity (African), place of residence (rural) and not having insurance. They did not find any association between educational level and marital status.

Ma et al. (2012) in China indicated that older age ( $\geq 55$  years), lower education (primary school education or illiterate), low annual income and being widow/divorced were the high risk factors for delayed reporting of cervical cancer.

In our study, socioeconomic condition of the family, degree of education, history of pop smear and smoking and addiction of husbands (i.e. passive smoking) had significant association with delay presentation of the disease.

Almost all of the studies in our investigated field have reported that literacy of women is considered as an independent risk factor for delayed diagnosis of the cancer. However, degree of education is indirectly linked with the average income, knowledge and understanding of nature of the disease, its related risk factors and health education (Galobardes et al., 2006; Franceschi et al., 2009; Lourenco et al., 2012). It is recommended to assess more educational programs regarding the importance of the cancer, its prevention and early diagnosis specially in population with low socioeconomic conditions.

**Brazil:** It is well established that the participation of patients in health related programs including screening or prevention activities is lower in those with lower socioeconomic status (SES). The association between SES and delayed cervical cancer diagnosis has been demonstrated in prior studies (Mitchell and McCormack, 1997; Lindau et al., 2002; McCarthy et al., 2010). The implication of this finding in our study is that the prevention or diagnostic programs should be target general population with more attention to those with lower socioeconomic conditions. Though in this study there was not significant relation between place of residence and delayed diagnosis of cervical cancer but it seems that this variables need to be investigated with larger sample size because both low educated and low SES are more prevalent among rural populations.

The association between smoking and passive smoking with cervical cancer has been reported in many studies. Accordingly passive smoking as a carcinogen potentially could progress transition of persistent

infection/preinvasive lesions to invasive cervical cancer. Though the mechanisms by which passive as well as active smoking induces cervical cancer is not understood clearly but possible mechanism is that tobacco smoke contains carcinogen which could cause immunosuppression and consequently progression of HPV infection to cancer (IARC, 2004; Louie et al., 2011). It seems that addiction could cause cervical cancer by similar mechanism. The lack of association between smoking of the patients and the cancer may be due to that smoking was not prevalent among Iranian women at that age. Considering the role of passive smoking and increased rate of smoking in developing countries and globally increasing trend of smoking in young females aged less than 20 (WHO, 2010), it seems that in order to perform appropriate cervical cancer prevention strategies effective tobacco control programs should be implemented.

In current study, there was significant relation between not doing Pap smear test and delayed diagnosis. Pap smear is considered the screening test of cervical cancer and has an important role in early detection, or prevention or delay in progression of cervical abnormalities to invasive cancer. It could result in significant decrease in cancer related morbidity and mortality. Many studies worldwide have studied the barriers related to poor utilization of Pap smear tests among women even in those countries with organized cervical cancer screening programs. Accordingly lack of knowledge and awareness about the cancer, its risk factors, its preventability and different cultural and geographical barriers are responsible in this regard (Chigbu and Aniebue, 2011; Bebis et al., 2012; Augusto et al., 2013; Maar et al., 2013). Though studies relieved that the barriers are presented even in women's with appropriate knowledge, but it seems that the most important barrier specially in our population is lack of knowledge about the cancer and its risk factors as well as its prevention. So considering the results of this study it is recommended to improve the women's knowledge in this regard using more comprehensive educational programs.

The limitations of current study were its cross sectional design and low sample size. It seems that in order to achieve more conclusive results further studies with larger sample size and prospective design is needed.

The results of this study indicated the risk factors related to delayed diagnosis of cervical cancer. Women with mentioned risk factors should be targeted for implementation of specialized educational programmes for improving knowledge and screening test. In addition the findings of this study could serve as baseline information for planning further large studies and performing large scale educational programs for general population. The consequences will be early detection, proper management and reducing disease related mortality.

## References

- Allgar VL, Neal RD (2005). Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. *Br J Cancer*, **92**, 1959-70.
- Arbyn M, Castellsague X, de Sanjose S, et al (2011). Worldwide burden of cervical cancer in 2008. *Ann Oncol*, **22**, 2675-86.
- Augusto EF, Rosa ML, Cavalcanti SM, Oliveira LH (2013). Barriers to cervical cancer screening in women attending the family medical program in Niteroi, Rio de Janeiro. *Arch Gynecol Obstet*, **287**, 53-8.
- Bebis H, Reis N, Yavan T, et al (2012). Effect of health education about cervical cancer and papanicolaou testing on the behavior, knowledge, and beliefs of Turkish women. *Int J Gynecol Cancer*, **22**, 1407-12.
- Benedet JH, Bender H, Jones H 3<sup>rd</sup>, Ngan HY, Pecorelli S (2000). FIGO staging classifications and clinical practice guidelines in management of gynecologic cancer. FIGO committee on gynecologic oncology. *Int J Gynaecol Obstet*, **70**, 209-62.
- Berraho M, Obtel M, Bendahhou K, et al (2012). Sociodemographic factors and delay in the diagnosis of cervical cancer in Morocco. *Pan Afr Med J*, **12**, 14.
- Brewer N, Pearce N, Jeffreys M, White P, Ellison-Loschmann L (2009). Demographic differences in stage at diagnosis and cervical cancer survival in New Zealand, 1994-2005. *J Womens Health (Larchmt)*, **18**, 955-63.
- California Office of Environmental Health Hazard Assessment (1997). Health effects of exposure to environmental tobacco smoke. California environmental protection agency. Sacramento, CA.
- Chigbu CO, Aniebue U (2011). Why southeastern Nigerian women who are aware of cervical cancer screening do not go for cervical cancer screening. *Int J Gynecol Cancer*, **21**, 1282-6.
- Devi BC, Tang TS, Corbex M (2007). Reducing by half the percentage of late-stage presentation for breast and cervix cancer over 4 years: a pilot study of clinical downstaging in Sarawak, Malaysia. *Ann Oncol*, **18**, 1172-6.
- Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*, **127**, 2893-917.
- Franceschi S, Plummer M, Clifford G, et al (2009). International agency for research on cancer multicentric cervical cancer study groups; international agency for research on cancer human papillomavirus prevalence surveys study group. Differences in the risk of cervical cancer and human papillomavirus infection by education level. *Br J Cancer*, **101**, 865-70.
- Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G (2006). Indicators of socioeconomic position (part 2). *J Epidemiol Community Health*, **60**, 95-101.
- Gyenwali D, Khanal G, Paudel R, et al (2014). Estimates of delays in diagnosis of cervical cancer in Nepal. *BMC Women's Health*, **14**, 29.
- Gyenwali D, Pariyar J, Oonta SR (2013). Factors associated with late diagnosis of cervical cancer in Nepal. *Asian Pac J Cancer Prev*, **14**, 4373-7.
- Hansen RP, Olesen F, Sorensen HT, Sokolowski I, Sondergaard J (2008). Socioeconomic patient characteristics predict delay in cancer diagnosis:a Danish cohort study. *BMC Health Serv Res*, **8**, 49.
- IARC (2004). Tobacco smoking and involuntary smoking. Lyon, France: IARC.
- Ibfelt E, Kjær SK, Johansen C, et al (2012). Socioeconomic position and stage of cervical cancer in Danish women diagnosed 2005 to 2009. *Cancer Epidemiol Biomarkers Prev*, **21**, 835-42.
- Ibrahim A, Rasch V, Pukkala E, Aro AR (2011). Predictors of cervical cancer being at an advanced stage at diagnosis in Sudan. *Int J Womens Health*, **3**, 385-9.
- Jemal A, Bray F, Center MM, et al (2011). Global cancer statistics. *CA Cancer J Clin*, **61**, 69-90.
- Khorasanizadeh F, Hassanloo J, Khaksar N, et al (2013). Epidemiology of cervical cancer and human papilloma

- virus infection among Iranian women-analyses of national data and systematic review of the literature. *Gynecol Oncol*, **128**, 277-81.
- Lindau ST, Tomori C, Lyons T, et al (2002). The association of health literacy with cervical cancer prevention knowledge and health behaviors in a multiethnic cohort of women. *Am J Obstet Gynecol*, **186**, 938-43.
- Louie KS, Castellsague X, de Sanjose S, et al (2011). International agency for research on cancer multicenter cervical cancer study group. smoking and passive smoking in cervical cancer risk: pooled analysis of couples from the IARC multicentric case-control studies. *Cancer Epidemiol Biomarkers Prev*, **20**, 1379-90.
- Loureiro AV, Fregnani CM, Silva PC, Latorre MR, Fregnani JH (2012). Why are women with cervical cancer not being diagnosed in preinvasive phase? an analysis of risk factors using a hierarchical model. *Int J Gynecol Cancer*, **22**, 645-53.
- Ma J, Zhu Q, Han S, Zhang Y, Ou W, Wang H, Zhao J, Liu Z (2012). Effect of socio-economic factors on delayed access to health care among Chinese cervical cancer patients with late rectal complications after radiotherapy. *Gynecol Oncol*, **124**, 395-8.
- Maar M1, Burchell A, Little J, et al (2013). A qualitative study of provider perspectives of structural barriers to cervical cancer screening among first nations women. *Womens Health Issues*, **23**, 319-25.
- McCarthy AM, Dumanovsky T, Visvanathan K, Kahn AR, Schymura MJ (2010). Racial/ethnic and socioeconomic disparities in mortality among women diagnosed with cervical cancer in New York City, 1995-2006. *Cancer Causes Control*, **21**, 1645-55.
- Mitchell JB, McCormack LA (1997). Time trends in late stage diagnosis of cervical cancer. Differences by race-/ethnicity and income. *Med Care*, **35**, 1220-4.
- Tanturovski D, Zafirova E, Stojovski M, Basheska N, Jovanovska V (2013). Impact of socio-demographic factors on the delayed diagnosis and advanced stage presentation of patients with invasive cervical cancer in Macedonia. *Prilozi*, **34**, 71-8.
- Thomson C, Forman D (2009). Cancer survival in England and the influence of early diagnosis: what can we learn from recent EUROCARE results and quest. *Br J Cancer*, **101**, 102-9.
- U.S. Department of Health and Human Services (2006). the health consequences of involuntary exposure to tobacco smoke: a report of the surgeon general. u.s. department of health and human services, centers for disease control and prevention, coordinating center for health promotion, national center for chronic disease prevention and health promotion, office on smoking and health. Atlanta, GA.
- Vinh-Hung V, Bourgain C, Vlastos G, et al (2007). Prognostic value of histopathology and trends in cervical cancer: a SEER population study. *BMC Cancer*, **7**, 164.
- World Health Organization (2010). Gender, women, and the tobacco epidemic. Geneva, Switzerland: World Health Organization.
- Yu CK, Chiu C, McCormack M, Olaitan A (2005). Delayed diagnosis of cervical cancer in young women. *J Obstet Gynaecol*, **25**, 367-70.