

Cervical cancer in Pakistan: A review

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Abstract

Cervix carcinoma is the second commonest condition in women under 50 years of age and third after breast and oral cavity cancers across all age groups. Though a preventable disease, the mortality rate is very high because it is an ignored ailment in Pakistan in terms of screening, prevention and vaccination. More than 70% of cancer patients report with very advanced stage of malignancy and this is the cause of the high rate of mortality in Pakistan. We covered studies cited during the previous 11 years (2005-2015) that reviewed many aspects of cervical cancer in Pakistan, including epidemiology, risk factors, screening test and their barriers, clinical presentation and prevention. Our analysis indicated that infections associated with human papillomavirus posed the greatest risk of carcinoma and consequent mortality rate, especially because of low socioeconomic status and poor knowledge of screening. Emphasis is laid on a need to organise proper screening programme taking into account what already is known about Pakistani women.

Keywords: HPV, Risk factors of cervical cancer, Pap smear, Screening, Cervix carcinoma.

Introduction

Carcinoma of cervix is a killing and growing cancer in Pakistani women of all ages. Approximately 500,000 women are diagnosed with invasive cancer of the cervix per year throughout the world,¹ killing 273000 women. Most affected females of cervical cancer are present in developing countries.² The exact rate of incidence and prevalence of cervical cancer is not known in Pakistan because it is an ignored disease in terms of screening and prevention. Inconsistence epidemiological data is available in different studies because of small-scale studies, limited population and dealing with only registered cases. In one previous study cervical cancer was rated as the fifth most common malignancy during 1977-1988, but it became the ninth most common in 1992-2001.³ Many studies reported that cervical cancer is included amongst the first 10 common cancers.^{4,5} In 2002,

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the prevalence of cervical cancer in Pakistani women was 0.009% (9/100,000) while in 2008 it was 0.019% (19.5/100,000), according to advance research started by the World Health Organisation (WHO).⁶ The prevalence of cervical cancer has risen in Pakistan where almost 20 women fall victim to cervical cancer daily, making it one of the top 10 countries with the highest female mortality rates.⁶ Some half-a-million women will die due to cervix carcinoma by 2030, according to WHO, and more than 98% of these deaths are likely to occur in developing countries like Pakistan.⁷

Risk factors

Risk factors can be categorised under unprotected and early sex, poor socioeconomic status, early reproductive cycles and multiparity, HPV infection, co-infections, hormonal altered immune system, smoking and low education level etc.^{8,9} Nausheen et al. observed that the 50% of smokers developed dysplasia.¹⁰ A cross-sectional study carried out in three hospitals in Punjab revealed that cancer was common in poor people (72.7%) and those who lived in rural areas (59%).¹¹ A study published in June 2013 found that the frequency and percentage of low socioeconomic status were more 7(58.33%) than other risk factors in cervical intraepithelial neoplasia patients.¹² Jahan et al. made assessment of risk factors of 103 female patients at Aga Khan University Hospital (AKUH), Karachi. Early marriages proved to be a detrimental factor in young girls, and as age crossed 26 years, the chance of abnormality decreased. In that study, 2.9% of patient's husband/partner was uncircumcised and 17.6% patients were below matric,¹³ increasing the risk because male circumcision was believed to save women from development of cervical tumour, and education has impact on parity, perineal hygiene and contraceptive choice to judge health opportunity and health-seeking behaviour. Today young girls are at more risk levels than before and high incidence rate was observed especially in younger women with an advanced stage of disease.¹⁴ Hasan et al. found that the association of glutathione-S-transferase Mu 1 null genotype in cervical cells with increased risk of squamous carcinoma of cervix.¹⁵ There are several other studies in this regard (Table-1). Human papilloma virus is a well-known sexually transmitted virus.¹⁸ The prevalence of HPV is high in Pakistani women with precancerous lesion of cervix and

Table-1: Risk factors of cervical cancer in Pakistan.

	Low socioeconomic Status	Use of OCP	Age at first coitus >20 years	No. of marriage self >1	Smoking
Das CM et al. ⁸	90.6%	12.5%	96.87%	56.25%	34.25%
Parveen S et al. ¹⁶	93 %	22%	not studied	39%	17 %
Sohail R et al. ¹⁷	44.8%	12.8%	43.3%	not studied	5.6%

OCP: Oral contraceptive pills.

Table-2: Prevalence of different genotypes of HPV infection from detected cases.

	Summary	HPV detection	HPV 16	HPV18
Khan S et al. ²²	60 samples analyzed from two tertiary care hospitals in Karachi.	98.3%	93.3%	1.66%
Yousuf S et al. ²³	50 samples of squamous cell carcinoma of cervix from 2 pathology laboratories.	18%	55.6%	0%
Siddiqua A et al. ²⁴	77 cervical samples were collected from major hospitals in Punjab.	94.8%	24.6%	24.6%
Gul S et al. ²⁵	67 samples of cervical cancer biopsies from government hospitals in Islamabad & Rawalpindi.	77.6%	44.8%	32.8%

HPV: Human papillomavirus.

HPV positivity up to 88% in invasive cervical cancer.^{19,20} Polymerase chain reaction (PCR) is a sensitive technique for the detection of HPV infection.²¹ Many biological and epidemiological studies proved that the involvement of HPV in successful progression of cervical cancer (Table-2). A major problem in evaluating the epidemiology of HPV in Pakistan is social ban on all affairs relating to sex and counting sexually-transmitted infections.

Pap smear and Barriers to Screening Test in Pakistan

Pap smear is an easy and extremely powerful method for identification of precancerous cervical disease. A study was carried out at Department of Pathology and Microbiology of The Aga Khan University Karachi, where 29 Pap smears were normal and 28 were abnormal out of 57 (22 showed abnormalities on cytology where as 6 showed atypical abnormal cells on Pap smear).²⁶ In a study of 546 smears, of these 302 showed inflammatory changes, 124 were normal, 40 were atrophic, 17 showed dysplastic changes, in which 10 showed low grade squamous intraepithelial lesion and 7 patients were of high grade squamous intraepithelial lesion. Eleven cases of carcinoma in situ and 52 smears were not enough to

detect result.²⁷ Several studies have observed a relation between cervical cancer and cervix abnormal cells detected on Pap smear (Table-3). Scattered work to seek better techniques for the diagnosis of this cancer, a study carried out in tertiary care hospital, Islamabad reported that visual inspection of cervix with acetic acid (VIA) has comparable more sensitivity 78.5% than Pap smear 61.1%.³² In Pakistan for cervix carcinoma VIA is a best substitute to cytological screening.³³ Screening coverage women related diseases is too low in developing countries. Screening barriers include poor knowledge about disease, lack of awareness of preventive health care, impossible to reach economic and geographic service, shy nature of women and lack of encouragement from communities and family. Approximately 70.1% of Pakistani women were ignored this malignant and only 4.3% of women were vaccinated against this cancer. Majority medical professional did not know about exact position of cervical cancer in body.³⁴ Mazahir et al. found that only 14% volunteers realized that the early diagnosis of tumour is possible by screening.³⁵ In one study, Imam et al. reported that 50.5% of females have never heard about Pap smear and 37.5% of participants thought that they had no need to get smear test.³⁶ A survey in tertiary

Table-3: Results of Pap smear test in Pakistan.

	Normal	Inflammatory	Dysplasia 1 or 1&2	CIN III specimen	Inadequate
Khattak ST. et al. ²⁸	61.6%	32%	1.66%	0.6%	1.33%
Khan I. et al. ²⁹	38.1%	55 %	1.2%	0.6%	1.9%
Haider G. et al. ³⁰	18.34%	75.33%	2.14%	1.12%	2.24%
Noreen R. et al. ³¹	35.7%	55.7%	3.3%	0.4%	5.0%

CIN III: Cervical Intraepithelial Neoplasia Stage III.

care hospital of Karachi was conducted to determine the information and recognition about different features of cervix carcinoma. Only 37 out of 393 persons (9.4%) knew about vaccine against HPV. Other aspects of the survey concluded that 54% of both nurses and interns knew about screening test (Pap smear) while 8% (biopsy), 2% (High Vaginal Swab), 3% (ultrasound) and 10% (radiological scans) were incorrect answers. Only 10% of nurses knew about Pakistani guidelines, that screenings recommended after 3 years not yearly.⁹ This study showed poor knowledge of vaccine and screening test even amongst health professions. Unfortunately, in Pakistan Pap screening has not been implemented as an organized way. Awareness regarding the vaccine and screening test has spread to Pakistan but there still remains a long way to go before it is included in regular medical practice.

Clinical Presentation and Prevention

More than 70 % of patients were reported with advance stages of malignancy in Pakistan.³⁷ Aziz et al. discussed a retrospective study of 167 female patients who presented with different types of genital neoplasia, out of 167, 56(33.5%) were of cervical cancer identified at the Nuclear Institute of Medicine and Radiotherapy, Jamshoro, Sindh. Only 8(14.28%) cases presented with stage I, and 42 (74.99%) cases were identified with stage II and III. Irregular vaginal bleeding 27(48.21%), vaginal discharge 25(44.64%) and postmenopausal bleeding 17(30.35%) were most common symptoms of patients.³⁸ Late stage diagnoses reduced the survival rate as was reported in Parveen's paper where 100% patients died after 5 years of diagnosis with stage IV.¹⁶ The treatment of carcinoma in earlier stage yields better outcomes, so the clinical stage at the time of identification is very important. Another study was conducted at a comprehensive cancer diagnostic and treatment facility in Lahore, and found that 67% patients presented with advanced stage II to IV and only 12% presented with stage 0 to 1.³⁹ Cervix carcinoma prevention can be classified as primary and secondary. Primary prevention includes vaccination of young girls while secondary level provides facility of screening test. Globally two vaccines, Cervarix and Gardasil, have been recommended to prevent the HPV spread. Number of randomised clinical trials confirmed that the prophylactic vaccine was useful in HPV infection.⁴⁰ Vaccination of younger women before marriage is the most effective preventive measure, as reported by WHO. Regular Pap smears, safe sex method, lowering the number of sexual partners, HPV vaccination and termination of smoking are included in preventive measures.⁴¹ Pakistan should implement the WHO strategy for primary prevention with HPV vaccination and

establish planned Pap smear screening operations all over the country.⁴²

We also recommend that screening test should be used as a regular test for all sexually active women in developing countries like Pakistan; prophylactic HPV vaccination to young girls should be included in the national immunisation programme; and the HPV vaccination programme should be reformulated and implemented in collaboration with WHO.

Conclusion

The increasing trend of cervix carcinoma, its identification at advanced stage, increasing cost of treatment with poor survival rate and poor knowledge about screening have increased the burden of carcinoma of cervix. Although the incidence of cervix carcinoma in Pakistan is lower than other western countries, but mortality rate is high due to scarcity of awareness, unavailability of Pap smear test, lack of follow-up and late presentation of cervical cancers. Late-stage diagnosed condition needs implementation of screening programme on the national level and to enhance the public health education to save the lives of Pakistani women.

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