PAP SMEAR STUDY FOR CERVICAL CANCER SCREENING AND ITS ASSOCIATED RISK FACTORS IN POSITIVE CASES

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ABSTRACT

Background Objective: Cervical cancer is the second most common cancer in women worldwide after breast cancer. It is one of the most preventable and curable of all cancer. The objective of this study was to screen the women for precancerous cervical changes and to evaluate their associated risk factors.

Material and Methods: This is prospective cross-sectional hospital based study conducted in 2 hospitals from Jan 2011 to Dec 2013. Married women aged 20-55 who presented to Gynae OPD after informed consent was included in the study. Exclusion criteria were pregnancy, acute pelvic infection, heavy vaginal bleeding and history of hysterectomy.

Results: Out of 1,000 women in which pap smear were taken, 240 lost to follow up. Out of 760 patient pap smear were normal in 170 (22.3%) patients. In 547 (71.9%) patients pap smear showed inflammatory changes. Atrophic changes were seen in 13 patients. Patients with positive changes were 14 (1.84%). Out these 8 (1.05%) were showing ASCUS, 2 (0.26%) patients with CIN I, 2 (0.26%) patient with CIN II and 1 (0.13%) with CIN III and 1 patient with squamous cell carcinoma.

Conclusion: Pap smear has proven to save lives by early diagnosis. There is definite possibility of primary prevention approach by life style modification through health education about the cervical cancer and its associated risk factors highlighting the importance of increase in the age of marriage, screening program in hospital should be mandatory especially targeting specific age group for detecting precancerous condition before they progress to invasive cancer. The role of vaccine for HPV should be emphasized.

Key words: Cervical cancer, pap smear screening, associated risk factors, primary prevention.

INTRODUCTION

Cervical cancer is the most common cancer in women worldwide after breast and oral cavity cancer, and in developing countries this cancer represents the leading cause of death.

The global burden of invasive cervical cancer is 500,000 new cases every year with 273,000 women dying of it globally i-e one death every 2 minutes. About 80% of deaths relate to cervical cancer occur in developing countries1.

The prevalence of cervical cancer has risen in Pakistan where about 20 women fall victims to cervical cancer daily, making it one of the top ten countries with the highest female mortality rate.2 A 2008 study by GLOBOCON, a WHO project of cancer related research reveals Pakistan's cervical cancer incidence was 19.5/100,000 in 2008 was compared to less than 9/100,000 in 2002, a clearly a rising trend. According to another study, more than 70% of patients were reported with advance stages of malignancy in Pakistan.3

Epidemiological studies demonstrate that the major risk factors are HPV infection, high parity, increasing number of sexual partners, young age at first inter course, low socioeconomic status and positive smoking history. Insufficient demographic information is available about the risk factors from population in Pakistan.

Cervical cancer is one of the most preventable and curable of all cancers. The pap smear is the standard screening test used to test for the presence of abnormal cells that could become cancerous. A regular pap smear provides an opportunity to detect precancerous cells in the cervix. Cervical cancer develops as a result of persistent infection with a HPV infection, a sexually transmitted virus. HPV infection has a high spontaneous clearance irrespective of age. Since small fraction of HPV infected CINs progresses to invasive cancer after a long latent period, and some additional risk factors which may be genetic, immunological and sociodemographic may play a role making a persistent infection4. Some reports that host inflammatory system and cell mediated immunity serves important role in determining whether HPV infection persist, regress or progress5. The longer the infection lasts the more it increases the possibility that it will continue and cause precancer/cancer. In 20-30% of females persistent infection over 12 months period have led to CIN II.6

The pap smear has proved valuable for mass screening and enabling lesions detection at an early stage for effective treatment and has an incidence of reducing squamous ICC by at least 80%. The pap smear does have its limitations, among them the most important being its 47-62% limited sensitivity and the subjective interpretation of the results.6 This study was conducted to find the frequency of pre-invasive lesions of cervical cancer and its associated risk factors in positive cases.

PATIENTS AND METHODS

It is a hospital based prospective cross-sectional study conducted to screen for the precancerous cervical changes and evaluate their associated factors. The study was conducted in Mansoorah Trust Teaching Hospital and Akhtar Saeed Trust Teaching Hospital from January 2011 to December 2013.

All married women aged 20-55years who presented to the gynae outpatient with gynecological problems, who gave consent for participation in the study were included. Patient's information was recorded on Performa.

Women who were pregnant, had acute pelvic infection, heavy vaginal bleeding and history of hysterectomy were excluded from study.

Cervical smears were taken with standard procedure, slides were prepared, labeled and fixed with 95% ethyl alcohol and stained by PAP stain and cytology was reported according to Bethesda system.

RESULTS

Cervical smear was taken from one thousand women attending the gynae outdoor after informed consent. Out of one thousand women 240 lost to follow up. Among the remaining 760 patients, cervical smear of 170 (22.3%) patients were reported as normal.

In 547 (71.97%) patients smear was showing inflammatory changes. Atrophic changes were seen in 13 (1.7%) patients. In 16 (2.1%) patients smear was inadequate due to blood staining and artifact.

Patients with pre-invasive changes were 14 (1.84%) out of those 8 (1.05%) were showing borderline nuclear abnormalities (ASCUS), 2 (0.26%) patients with CIN I, 2 (0.26%) patients with CIN II, and 1 (0.13%) with CIN III and 1 (0.13%) with squamous cell carcinoma (SCC).

DISCUSSION

Cervical cancer has been a major cause of morbidity and mortality in parts of developing world where pap smear screening is not available.

No accurate figures exist for the prevalence and mortality of cervical cancer in Pakistan because of inadequate pap smear screening programs and lack of system for registering cancer cases in hospital settings. Furthermore social taboos associated with sexually transmitted diseases also hinder women from coming forward to undergo requisite test and treatment. Our study showed that there were 98.15% benign and inflammatory smears and 1.84% was premalignant and malignant lesions.

n=760 Age group (in Years)	20-30	31-40	41- 50	≥ 50	Total (%)
Normal	75	54	30	11	170 (22.3%)
Inadequate	06	05	03	02	16 (2.1%)
Inflammatory changes	236	219	60	32	547 (71.97%)
Atrophic changes	0	03	06	04	13 (1.7%)
Border line nuclear abnormalities (ASCUS)	01	04	03	0	08 (1.05%)
AGUS	0	0	0	0	0
Mild dyskaryosis CIN I (LSIL)	0	01	01	0	02 (0.26%)
Moderate dyskaryosis CIN II (HSIL)	0	01	01	0	02 (0.2%)
Sever dyskaryosis CIN III (HSIL)	0	01	0	0	01 (0.13%)
Squamous cell carcinoma (SCC)	0	0	01	0	01 (0.13%)
Total	318	288	105	49	760

 Table 1: Relation of age with various non-neoplastic and neoplastic pathology of cervix

n=14 Characteristics	No %
Age at 1st marriage	
< 18	
18-20	
>20	
6 (42.85%)	
5 (35.7%)	
3 (21.4%)	
Parity	2 (14.2%)
P0-P3	8 (57.1%)
P4-P6	4 (28.5%)
Parity ≥ 7	
No of marriages of both partner	10 (71.4%)
Patient	4 (28.5%)
1	
2	
Spouse	9 (64.2%)
1	5 (35.7%)
2	
History of smoking	4 (28.5%)
Smoker	10 (71.42%)
Nonsmoker	
History of contraception	2 (14.2%)
Condoms	3 (21.42%)
OCPs	7 (50%)
No contraception	1 (7.14%)
IUCD	1 (7.14%)
Tubal ligation	
Socioeconomic status	12(85.7%)
Lower	2(14.28%)
Middle	0(0%)
Upper	

Table 2: Demographic characteristics in positive cases

ASCUS was found to be highest in the age group 31 - 50 years in this study. ASCUS has incidence of 1.05% while AGUS was not detected. Ratio of inflammatory and other lesions to premalignant and malignant one was 746:14 (98.1% and 1.84%), positive cases in this study were 14(1.84%). These figures can be compared with one study in Saudi Arabia showing positive cases around 1.66% and local study by Rasul et al. showing positive cases of 1.3%. And a local study at Lahore general hospital with figures of 1.3%.7In our study patients with moderate to severe dyskaryosis were in the 4th decade of life which was also observed in one Australian study.8

In our study out of positive cases 78.57% of female were <20 years of age. Another local study conducted at MINAR cancer hospital in Multan also showed that 88% cases were married at less than 18 years.9 The relationship of cervical cancer with sexual behaviour is supported by the fact that disease is rare in nuns. The first review of literature on the risk factors associated with sexual behaviour was published in 1967 which reviewed nine studies. The main factors explored were early age at marriage, marriage dissolution and remarriage. In all the studies the percentage of women having marriage before 20 years was significantly higher than controls.10

Early age at first sexual intercourse, early age at first pregnancy and high parity make women weaken physically and immunologically for latent HPV infection which may lead to cervical carcinogenesis as women get old. As a result of multiple exposures to carcinogenic substances and microbes over the period of years this accumulates and may involve in alteration of gene expression.11

Immature cervix during adolescence is more susceptible to persistent HPV infection therefore has a greater risk of cancer development. IARC multicentric case control study in 2002 proved a direct association between the number of full term pregnancies and squamous cell cancer risk.

Since HPV is sexually transmitted hence the sexual behaviour, number of sexual partners of the woman and her partner both notably impact the risk of invasive cervical lesion (ICC). Some studies show that the male circumcision reduces the risk of ICC in female partners.12,13The risk of development of cervical cancer is elevated by 2 to 4 times if a woman reports having more than one contact.10 The risk of cervical cancer is influenced not only by woman's sexual behaviour but also by male sexual behaviour. Poor penile hygiene of male partners has also been hypothesized as a risk factor for cervical cancer.14 In our study out of positive cases 28.5% of the patients were married twice and 35.7% of husbands of the patients were married twice. All patients were muslim and their partners were circumcised and majority of them belong to low socio-economic status. A crosssectional 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%).15

The evidence for the casual role of HPV in the development of cervical neoplasm comes from observational and epidemiological studies. The epidemiological data strongly support that HPV infection is a primary risk factor. Majority of studies have revealed that HPV infection of type 16 and 18 in emergence as a primary risk factor for cervical cancer. Recent studies have indicated that high parity becomes a risk factor in the development of CIN III or invasive lesion in the presence of HPV.11,16

Regarding family planning practices, use of OCPs is common particularly in the west. Recent investigations have raised concern for the long-term users. Majority of the studies have revealed high risk of neoplasm with increasing use of pill.17 Barrier method of contraception has been recommended as the preventive measure for cervical cancer possibly because it offers protection against some of the STDs. In this study 21.4% of patients were using oral contraception pills & 14.2% were using condom, 50% of patients were non-users.

Tobacco use has also been considered as an important risk factor because smoking is related in causing defects in DNA repair system in biological cell and leads to carcinogenesis, and DNA damage has also been found in cervical tissue of smokers. Same kind of results also found in meta-analysis study where it showed that the risk of squamous cell cervical cancer is increased by 50% in current smokers.18,19 Moreover passive smoking also plays a significant role in cervical carcinogenesis. Nausheen et al. observed that the 50% of smokers developed dysplasia.20 In our study out of positive cases 28.57% of patients were smokers.

CONCLUSION

Pap smear is an inexpensive test that has proven to save lives by early diagnosis. In Pakistan we have predominant rural population having low socioeconomic status with inadequate medical facility and custom of marriage at an early age. So, it is a major challenge to organized mass scale screening in Pakistan hence the alternatives are needed to be worked out.

There is a definite possibility of primary prevention approach by doing life style modification, health education about the cervical cancer and its associated risk factors, highlighting the importance of increase in the age of marriage, regular screening and vaccination of young girls. Screening program should be mandatory in hospitals. They should specially target specific age group for detecting pre-cancer conditions before they progress to invasive cancer.

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