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ORIGINAL ARTICLE

Risk Factors for Invasive Cervical Cancer among Distinct Populations in Low Resource Countries

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ABSTRACT

Background: Cervical carcinoma is the commonly known leading malignancy that has the highest prevalence in the developing countries. It shares second rank in the world of cancer. The 80% of the cases of the cervical cancer in the developing countries are reported. It is reported that the one woman die from this cancer after every two minutes.

Objective: To identify the risk factors associated with the cervical carcinoma (CC). The role of human papillomavirus (HPV) in aetiology of cervical carcinoma was also evaluated.

Study design: It is a hospital based case-control study.

Material and Methods: The total 226 ICC cases were included in the study and 234 female were kept in control group. The study was conducted at the Divisional Headquarter Teaching Hospital of Mirpur AJK from May 2020 to May 2022. PCR was used for the evaluation of the HPV DNA in cervical cells. Multiple logistic models were used to compute the 95% confidence intervals CIs and odd ratios ORs. The all control women except one has the HPV infection.

Results: The all control women except one has the HPV infection. The HPV of 23 different types associated with the risk of ICC. The HPV 16 was present in most of the patients either belong to case or control group followed by the HPV 18 and 33. HPV 18 has stronger association with ICC. The odd ratio of the single infection was higher than the multiple infections. Other factors such like early menopause, high parity and husband extramarital sexual affairs are also associated with the ICC.

Conclusion: The HPV level is considered significant for the cervical carcinoma because of the lack of knowledge about other factors. A number of factors like socio-economic pressure, poor hygiene, menopause, education, and the sexual life of the husband of the patient play a major role in the carcinoma.

Keywords: Cervical cell carcinoma, risk factors, human papillomavirus (HPV), squamous cell carcinoma, adenocarcinoma.

INTRODUCTION

Cervical carcinoma is known to be the second most common cancer in the world. The women under 50 years of age are more prone to the development of cervical carcinoma. The highest morbidity and mortality rates are associated with the cancer[1-2]. The mortality rate are observed to be 273000 women per year. There is improper setup of screening and prevention of cervical carcinoma in Pakistan.

The HPV infection increases the mortality rate associated with the cervical carcinoma. It is the dominating factor that play significant role[3-4]. The poor socioeconomic status and knowledge are also the associated factors that are increasing the cervical carcinoma incidence. Proper screening of the cervical cancer is necessary. Limited knowledge about the cervical carcinoma is available. The prevalence of cervical cancer has increased in the past years in Pakistan[5-6]. It was observed to be 0.009% in 2002 and increased to 0.019% in 2008. The highest mortality rates in females are observed in Pakistan, these tend to be 20 women per day fall victim to this disorder. According to the WHO, the 0.5 million women will die from the cervical cancer. The developing countries like Pakistan account for more than 98% of such deaths[7-8].

Early sex and early reproductive cycle, hormonal effected immune system and poor socioeconomic conditions with lower education status and increased smoking habits are the risk factors of cervical carcinoma. The dysplasia is observed in almost 50% of the smokers. The poor people are more prone to the development of the cancer. The poor socioeconomic conditions also significantly increasing the incidence of ICC[9].

The young girls are more prone to development of carcinoma, than the old age women. The advanced stages of carcinoma are observed in the young girls. The other risk factor is glutathione-S-transferase Mu 1 null gwnotype[10-11].

HPV can be transmitted through sexual contact. The precancerous lesions of cervix are observed in the HPV associated carcinoma. Almost 88% cases of ICC are positive for HPV. The sensitive technique for detection of HPV is Polymerase Chain Reaction (PCR). The HPV involvement increase the progression of the cervical carcinoma. The all the affairs related to the sex are socially banned in the Pakistan, therefore it is difficult to evaluate the epidemiology of the cervical carcinoma. For identification of the precancerous cervical disease Pap smear screening test is also used[12].

This study was conducted to evaluate the role of different HPV in the progression of cervical carcinoma. The limited knowledge about the different risk factors is present; therefore study was conducted to determine the associated factor roles in ICC progression in the people living in low resource companies[13-14].

MATERIAL AND METHODS

The 226 ICC cases visited the divisional Headquarter Teaching Hospital of Mirpur AJK for six months from May 2020 to May 2022 were included in the study and 234 female were kept in control group. The informed consent was given to the each participant. According to the inclusion criteria the patients diagnosed with the ICC and haven't received any treatment for cancer were included. It was also observed that the patient don't have physical and mental impairments. The women who don't have the neoplastic lesions were excluded from the study. The fourteen women, who were diagnosed with cervical intra-epithelial neoplasia (CIN), were also excluded from the study.

According to the exclusion criteria for the control women the women diagnosed with ano-genital cancer were excluded from the study PCR with beta-globin gene specific primer was used for the evaluation of the HPV DNA in cervical cells. Multiple logistic models were used to compute the 95% confidence intervals CIs and odd ratios ORs. The all control women except one has the HPV infection. The patients having the history of the cervical conization with any physical or mental problem were also excluded. The pre-tested questionnaire was given to each patient. The ethical committee of the hospital approved the study. The pelvic examination was performed for every patient.

RESULTS

In this table, the infection by the HPV was identified in all of the cases except on ICC patient. For this study 226 patients were selected, and 234 female were kept in control group. The HPV was most common in female of the control group. The table also highlights the infection by HPV of several types associated with the risk of ICC. The multiple infections due to HPV is not much contagious as compared to the single way of infection.

Table 1: HPC disease in 210 patients of carcinoma of cervical and 202 control groups its OR and 95 % CI

	Carcinoma of cervical		Control group		
	No.	(%)	No.	(%)	OR (95 % CI)[2]
HPV					
Negative one	1	-0.51	146	-73.3	1
Positive of every type	209	-99.6	56	-28.7	498.9 (68.7–999.0)
Multiple Contagion					
No	176	-84.8	49	-22.9	1
Yes	33	-16.7	8	-4	1.3 (0.6–3)
Types of HPV					
HPV 16	126	-61.2	35	-18.4	1
HPV 18	30	-14.9	3	-1.5	3.8 (0.8–16.4)
HPV 18 and HPV 16	7	-3.6	3	-1.5	0.6 (0.3–3.7)
associated types of HPV 16	27	-14.1	1	-0.8	7.3 (0.7–52.4)
associated types of HPV 18	9	-4.5	4	-2.8	0.7 (0.3–3.0)
Other categories	10	-4.9	11	-5.5	0.4 (0.2–0.8)

For the comparison of rigidity of lined ICC with several types of HPV issue. All of these multiple infections by HPV is highlighted in the below table. In this table the women infected by HPV-16 was compared with the women infected with HPV-18 which leads to the increase in the level of OR. And all the types linked with HPV18 are also highlighted over here which leads to increase in the level of ICC.

Table 2: Carcinoma of cervical in 226 patients, and 234 of the control groups with regard to habit of sexuality and extramarital affairs

	No. of Cases (%)	Control groups (n, %)	95 % CI
first intercourse age in years			
≥22	22 (9.6)	37 (16.5)	1.0
18–21	40 (18.7)	45 (19.8)	1.5 (0.8–2.8)
18–19	61 (28.0)	73 (30.9)	1.4 (0.8–2.6)
16–17	51 (24.0)	44 (17.3)	1.8 (0.8–3.7)
<14	52 (23.6)	35 (15.2)	2.5 (1.3–4.9)
$\chi 2$ for trendline			5.50; p = 0.04
sexual partners no.			
1.0	215 (95.1)	230 (97.6)	1.0
≥3	11 (4.9)	4 (1.5)	4.0 (1.1–14.8)
sexual habits of husband			
Extramarital intercourse			
Not	67 (31.0)	172 (72.6)	1.0
Uncertainty	47 (22.2)	27 (11.0)	4.2 (2.6–7.7)
Yes ofcourse	110 (48.0)	35 (13.6)	8.8 (5.5–13.6)
Intercourse with unknowns			
No at all	69 (32.0)	183 (79.3)	1.0
Uncertainty	53 (22.7)	23 (98.9)	5.7 (3.3–11.6)
Yes ofcourse	103 (44.3)	27 (12.8)	10.6 (6.2–17.2)

Apart from the other factors involved in the carcinoma of the cervical, there are a number of other factors like age has much significance. The age of the person at the time of first intercourse is particularly important, it should be more than 15 years, and having sexual relations with more than 3 persons may also lead to the serious risk issues. This may lead to an increase in the level of ICC. The usage of oral contraceptives and devices of uterine have no serious link with this disease. In the case of contraceptive methodologies, tubal ligation is the most commonly employed method. If husbands of women develop extramarital affairs with the prostitutes, it causes the increased level of ICC and ultimately carcinoma of cervical. When the data of such activity was taken, then most of the women were not sure about it, and if the husband developed some sexually transmitted diseases, like syphilis or genital wrates, then women may develop the chances of carcinoma. No woman was found to be suffering from some sexually transmitted disorder.

DISCUSSION

It is assured from our study that, for the development of carcinoma of cervical, the HPV is present in the patients. All of the cases suffering from carcinoma of cervical had HPV except one patient. The types of HPV most commonly prevalent are HPV-16, HPV18, HPV33, HPV35, and HPV45. All these types of HPV may involve in the development of significant amount of carcinoma of cervical. This disease is particularly prevalent in Asian countries[15]. The infection rate of HPV among the women of control group was 27 %, and when all types of HPV were studied, it was noted the HPV16 and HPV18 are mostly involved to cause carcinoma of cervical (mainly hpv-16 play a major role) [16].

It is the most common disease in the middle age people, Due to multiple infection of HPV a number of issues raise in the population, but these issues was not related to increase in the level of ICC. The association of HPV 18 with the cervical carcinoma was considered most effective but HPV 16 have much crucial role. When the risk comparison of both of the strain was done, it was observed that, the HPV 18 is involved in causing some oncogenic effects in the cell lines, due to its high rate of prevalence. This study was not much elaborated to give complete information about the effect of rare types of HPV which may involve in causing carcinoma of the cervical[17-18].

A part from the HPV, which was considered as a sole reason of carcinoma, there are several other factors that may play their role in the initiation of carcinoma. Among these factors poverty, and sexual behavior of the husbands of infected females have play a major role. When epidemiological studies was carried out in the population suffering from some social and economic pressure, it was observed that most of these females are suffering from cervical cancer and a number of other types of tumors in the cervical region. But not all the women suffering from social and economic poverty may develop cervical cancer some of the high class women may also develop this disease[19-20].

In the case of women of high class, the sexual lives of their husbands play a major role. If husband have extra marital affair with more than 2 to 3 women or prostitutes, then there are chances that, he may develop some kind of sexually transmitted disease of urogenital tract or genital organ. Then intercourse with such an infected husband may also lead to carcinoma cancer or the cancer in the cervical region[21-22]. No woman infected with carcinoma of cervical was directly having some sexually transmitted disease. But the accurate data about this was not obtained because a lot of women was not aware of the extra marital affairs of their husband.

There are a number of other factors correlated with the carcinoma of the cervical, among these factors illiteracy, low nutrients level and poor hygiene also play its role for the prevalence of HPV. In this study, the poor hygiene is associated with the reason of HPV but this situation may not lead to an increase in the level of ICC. Smoking may seldom because HPV or the raising of ICC level, however, chewing of pan and other things may lead to cancer and cancer of cervical and other body parts. The women have less knowledge about the unhealthy diet are involved in eating such pan[23]. The women having pregnancy issues have some hormonal imbalance and labor induced issues may also have chances to develop some oncogenic issues in the cervical region. Usually, the lack of proper nutrients in such a situation may lead to serious issues and hormonal issues which may cause HPV as well during the child birth[24].

In short, when all the situations are considered in this study, it was observed that there is no proper information with regard to the sexual life style of the patients' husbands. Due to the lack of enough data, no appropriate prediction can be made about the involvement of sexuality in enhancing the level of ICC in the patients. However, lack of hygienic food and social and economic pressure has a major role in the initiation of carcinoma of cervical and HPV in the female[25].

CONCLUSION

The study concluded that at the present time HPV level may be considered for the carcinoma of cervical because of the lack of knowledge about other factors. A number of factors like socio-economic pressure, poor hygiene, menopause, education, and the sexual life of the husband of the patient play a major role in the carcinoma. About 30 % involvement of HPV 16 and HPV 18 is predicated to cause carcinoma.. Vaccine for this disease is still under development.

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