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HPV Infection and its Relation to Cervical Cancer Screening History and Other Risk Factors

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Abstract: ***Objectives:*** ***We conducted a study to investigate the prevalence of human papillomavirus (HPV) infections in an opportunistic. Sample of women in odissa, India. We inquired about risk factors associated with HPV infections and linked the HPV results with the cervical cancer screening history of the patients.*** ***Methods:*** ***The study population included 200 symptomatic and asymptomatic women patients attending Papanicolaou (Pap) test at AHRCC. After signing a consent form, patients were given a self-administered questionnaire (after approving by local ethics committee) on risk factors and received a conventional Pap test. Residual cells from the Pap tests were collected and sent for HPV testing.*** ***Results:*** ***The mean age of the population was 48 years. A total of 116patients (58.0%) had an HPV infection, 84 (42.0%) of whom had a normal Pap test or HPV -ve, 44(37.93%) were affected by hpv typing 16 and 18, which are mostly prevalent and 54(46.55%) had affected by multiple infection. Of those who were HPV positive, the most consistent risk factors were young age, higher number of pregnancy, low socio-economic status, diet, tobacco and living status. We cannot find any relation between cervical cancer risk factors with OCP and family history of patients of higher age.*** ***Conclusion:*** ***As Odissa is a socio-economically backward state of India, these data provide baseline information on HPV prevalence specially 16 and 18 in an unvaccinated population and can be useful in evaluating the effectiveness of the HPV immunization programs. An added benefit is in this study is a risk behavior survey to assess early and late outcomes of HPV infection, which is very helpful to save the life of women.***

Keywords: HPV, Pap tests, risk factors, , low socio-economic status

1. Introduction

Carcinoma of the cervix continues to be the second commonest female cancer worldwide with only breast cancer occurring more commonly while it is the commonest cancer occurring among females in developing countries. In the developing countries about 75% patients of carcinoma of cervix present with an advance stage. Cervix cancer is the most prevalent cancer in women after breast cancer. It is the most common cause of death among women of ages between 41 to 50 with gynaecological cancer. The causative factors for development of cervix cancer are many such as infection by certain viruses. Human papilloma viruses (HPV), age pregnancy, use of contraceptive pills, nutritional deficiencies and mode of different life styles (habits) etc. [etal 2012] In India approximately 71,600 new cases of cervical cancer are reported every year Odisha, One of the socio economically background states of India with illiteracy is suffering from high cancer incidence. Numerous studies of the epidemiology of cervical cancer have shown strong association with other risk factors for cervical cancer includes cigarette smoking and tobacco chewing. Cervical cancer is one of the most malignant diseases of women it is diagnosed in almost half a million women every year and half of many die from it annually. In India, its incidence has decreased due to cytological screening. Primary preventation can be achieved through health education and vaccination to prevent infection from HPV. (Human Papilloma virus). The objective of this study was to determine risk factors and the prevalence of HPV infections in the sample of women attending Papanicolaou (Pap) test.

2. Materials and Methods

In this study, 200 number of patients were studied from 2013 to 2014. These patients were referred by the Gynecological department of S.C.B. Medical College & Hospital to the Archarya Harihar Regional Cancer center. After approval by ethical committee in ARHCC, Odissa, patients were given a self-administered questionnaire on risk factors and received a conventional Pap test. Residual cells from the Pap tests were collected and sent for HPV testing. , samples in viral transport medium were centrifuged and their DNA extracted from the resulting pellet using a DNA extraction kit. The DNA was amplified with a nested polymerase chain reaction (PCR) method .PCR products were visually detected by gel electrophoresis. HPV DNA was detected and typed by hybridization to microspheres coupled to specific probes for the HPV types .HPV stain 16 or 18 was called as high risk types and 6,11,33,40 etc as low risk types.

3. Data Analysis

Screening history of the consenting participants were calculated by using Univariate and multivariate logistic regression analyses were used to calculate odds ratios (ORs) as estimates of the relative risk of HPV detection associated with the various predictor variables. By using odd ratio,95%CI were calculated and p value were find out to determine whether the variable were significant or not. Because of the higher prevalence of HPV in women aged less than 40 years, results were tabulated for women aged less than 40 years and for those aged 40 years plus. HPV infection results and survey results were linked in order to get the results of the Pap tests performed and the cervical cancer

4. Results

Table 1: Result by AGE and HPV Infection Status

Variables	*categories*		*AGE<40YRS*		*Result by Age and HPV Infection Status*					*Age>40 YRS*		*OR(95% CI)*	*P value*
			infection							*infection*			
		Total No.	*HPV(+ve)*		*HPV(-ve)*		*OR(95% CI)*	*P Value*	*HPV(+ve)*		*HPV(-ve)*		
			n	*%*	*n*	*%*			*n*	*%*	*n*	*%*	
	normal	*47*	*6*	*25.5*	*21*	*89.3*	*Reference*	-	*9*	*38.2*	*11*	*46.8*	*Reference*	-
	inflammation	43	9	41.8	11	51.1	4.81(1.33-17.40)	0.01	14	65.1	10	46.5	1.71(0.51-5.66)	0.37
	mild dysplasia	31	9	58.0	11	70.9	2.86(0.80-10.14)	0.10	3	19.3	8	51.6	0.45(0.09-2.25)	0.33
histology	moderate dysplasia	27	4	29.6	6	44.4	2.33(0.49-11.06)	0.28	8	59.2	9	66.6	1.08(0.29-3.97)	0.90
	severe dysplasia	31	4	25.8	7	45.1	2.0(0.43-9.21)	0.37	11	70.9	9	58.0	1.49(0.42-5.19)	0.52
	c.i.s	11	2	36.3	3	54.5	2.33(0.31-17.34)	0.40	3	54.5	3	54.5	1.22(0.19-7.59)	0.82
	invasive carcinoma	9	2	44.4	2	44.4	3.50(0.40-30-34)	0.25	3	66.6	2	44.4	1.83(0.24-13.47)	0.55
pregnancy	<3	70	11	31.4	27	77.1	Reference	-	7	20.0	32	91.4	Reference	-
	>3	130	21	32.3	31	47.7	1.83(0.24-13-47)	0.55	35	53.8	43	66.1	3.72(1.46-9.44)	0.01
economic status	middle	92	12	26.0	40	86.6	Reference	-	7	15.2	23	50.0	Reference	-
	poor	108	16	29.6	20	37.0	2.66(1.06-6.69)	0.03	28	51.8	44	81.4	2.09(0.79-5.51)	0.13
diet	veg.	74	9	24.3	22	59.4	Reference	-	7	18.9	36	97.2	Reference	-
	non veg.	126	36	57.1	51	80.9	1.72(0.71-4.18)	0.22	15	23.8	24	38.0	3.21(1.14-9.05)	0.02
tabbaco	yes	127	22	34.6	27	42.5	1.38(0.59-3.18)	0.44	38	59.8	40	62.9	2.57(0.97-6.82)	0.05
	no	73	14	38.3	33	90.4	Reference	-	7	19.1	19	52.0	Reference	-
family history	yes	72	23	63.8	29	80.5	0.49(0.21-1.10)	0.08	7	19.4	13	36.1	0.20(0.06-0.64)	0.00
	no	128	12	18.7	41	60.0	Reference	-	14	21.8	61	95.3	Reference	-
ocp	yes	82	25	60.9	42	102.4	1.25(0.59-2.65)	0.54	8	19.5	7	17.0	5.71(1.74-18.76)	0.00
	no	118	18	30.5	38	64.4	Reference	-	12	20.3	60	101.6	Reference	-
living status	rural	138	20	28.9	23	33.3	2.80(1.07-7.30)	0.03	48	69.5	47	68.1	2.48(0.94-6.52)	0.06
	urban	62	9	29.0	29		Reference	-	7	22.5	17	54.8	Reference	-

The mean age of the study population was 48 years. The mean age of HPV infected women was 35 years, and the mean age of HPV non-infected women was 45 years. The majority of patients came from rural areas (69.0%), and the remainder came from urban areas.[1]Variables associated with the infection using univariate analysis are reported in Table 1. Results are presented for women aged less than 40 years (referred to as “younger”) and for women aged 40 years and older (referred to as “older”) to reflect the higher prevalence of infections in older women.[2] .Taking patients Histology as a variable and normal control group as a reference group, compared with all histological types, we found ,all the values are significantly increases for both younger age and older age. Pregnancy below 3, taking as control group or reference group, compared to pregnancy above 3.It was found that, probability of HPV infection increases .p-value was significant for both younger and older groups. By comparing between economic status, we found all the variables are positively significant. Compared with non-smokers, participants who smoked were at greater risk of being infection-positive. Like that there is a positive co relation between tobacco chewing and cervical cancer [4]. The variables diet (veg/non-veg) also significantly co-related.[5] .

But we cannot find any positive co-relation between variables like family history and use of oral contraceptive pills user of older group.

5. HPV Infections and Cytological Outcomes

This study is based on the analysis of data regarding same 200 patients. Table-2 shows that a total 116 of were found to be HPV+ positive. Number of patients who were HPV -ve are 70.18 number of patients were affected HPV stain 16 or 18 and 18 of them were affected by low risk HPV like stain 6,11,13,32,40 etc.Out of them 54 numbers of patients were affected by multiple infection. Overall, 25.86(30/116*100) of these maximum infections were among 40-45 year of ages.

Table 2: Age Distribution of Women by HPV Infection Status

Age	*HPV +VE*	*% of HPV+VE*	*HPV -VE*	*% of HPV-VE*	*HPV 16or18*	*% of HPV 16or18*	*Low risk HPV*	*% of Low risk HPV*	*Multiple Infection*	*% of Multiple Infection*
>20	1	0.86	11	13.09	1	2.27	0	0.00	1	1.85
>25-30	11	9.48	7	8.33	7	15.90	3	16.66	1	1.85
30-35	9	7.75	8	9.52	5	11.36	2	11.11	2	3.70
35-40	18	15.51	7	8.33	5	11.36	3	16.66	9	16,16
40-45	30	25.86	3	3.57	9	20.40	4	22.22	17	31.48
45-50	26	22.41	8	9.52	8	18.18	3	16.66	15	27.77
50-55	8	6.89	10	20.83	3	6.81	1	5.55	4	7.40
55-60	10	8.62	16	19.04	4	9.09	2	11.11	4	7.40
>60	3	2.60	14	16.66	2	4.54	0	0.00	1	1.85
Total	116	-	84	-	44	-	18	-	54	-

The patients aged less than 25 years and 60 year were less likely to be infected with HPV. While HPV stain 16 or 18 were detected in women aged 40-45(20.20%), 25-30(15.90%), 45-50(18.18), 35-40(15.90) were very high. Multiple infections were more in an age group of 40-45(31.48).

6. Discussion

A number of cofactors are associated with risk of having an infection and different grades of cervical abnormalities, many of which are related to sexual behaviours. Our study suggest that, cofactors for HPV infection including age , smoking, oral contraceptive use, chewing tobacco, high pregnancy, low socio-economic status, family history of cervical cancer etc. Our present study also suggests that some of these risk factors are common for all age groups while other factors are found only in either younger or older women.

In the present study, women between 40-45 years of age and older with no Pap test history were found to be HPV infection-positive more often. pooled data(table-1) compared to women who had never given birth or less given birth, those with three or more full term pregnancies had more times the risk of developing cervical cancer, women with seven or more births had the high risk.[7] Other studies corroborate this positive relationship found between high parity and cervical cancer[7,8]. The physiologic reason for the association is unclear; possibilities include hormonal factors related to pregnancy or cervical trauma associated with delivery. In our present study, high parity was the prominent finding. These finding shows, women with gynaecological cancer had more than one pregnancy during their lives. This finding is completes agreement with studies by Kjaer in Denmark [9], Gharono in Benin city- Nigeria [10] , Latifa Shamsuddin in Bangladesh [11,12] and Muhammed Ikram in Lahore[13].

In the present study, smoking and use of oral contraceptive pills (OCPS) are also important risk factors. Our present study collaborates with the study of Kjaer in Denmark, in which smoking and oral contractive use were important risk factors. In other study, it was found that, smoking appears to be strongly associated with the development of precancerous cervical lesions and cancer [14,15] studies shows at least a twofold, risk factor current smokers compared to non-smokers. But in our present study, unfortunately we cannot find any positive co-relation between OCPS and cervical cancer in older ages.[16,17]

Low Socio-Economic Status (SEC) is recognized as a risk factor for many health problems, including cervical cancer, particularly in low-resources settings, women with low SES often have limited income, restricted access to health care services, poor nutrition, and a low level of awareness about health issues and preventive behaviour. All of these factors can make them more vulnerable. In our present study, 54.0% patients belonged to low socio-economic or poor classes where as 46.0% belonged to middle classes. These findings are slightly different to those Varghese et al, in which 57% of the patients were in the low income category whose monthly income was under one thousand per month. But if the criteria for low socio-economic group are select as under use of BPL cards, in this study, both the studies may coincide. This study coincides with the study by Gharoro et al4 in which poverty featured prominently. Responsible to illness and preventable diseases such as cervical cancer. While some researchers have speculated that poor hygienic practices or conditions may increase risk of cervical infection, but there is no consistent evidence to support this assertion.

In our present study the peak incidence of carcinoma of the cervix was found in age group 41-45 years. This observation is similar to those of Riaz Ahmed Bhutta et al and Roohi and Sahi. But differ from Parveen et al and Latifa Shamsuddin et all who reported more cases in early age groups. The number of cases after the age of 60 years and above is less in this study as compared to those of Dumn and Schweitzr and EI-Senoussi et al. This difference may be due to less life expectancy in our country.

In our present study, 69% of the patients are rural and non-employed. Probably, due to poor hygiene conditions i.e. absence of genital washing and use of sanitary napkins were mostly affected by cervical disorder and inflammatory diseases.

In our study, we found a +ve co-relation between HPV and family history of patients in younger age group, but we cannot co-relate HPV and family history of higher age group. Besides these all risk factors, the role of nutritional status to risk cervical neoplasia has been of recent interest. Initial case control studies in New York state and in Italy suggested a protective effect of vegetables and fruits rich in carotenoids on cervical cancer. We also agree with this because in our present study, we found that many patients about 63% who were affected by cervical cancer were non-vegetarians. So, we think that, diatary intake also likely to be a factor for cervical cancer.

From our present study(table-2) two, it was found that, HPV infection more often prevalence in the age group of 40-45 and it s lowest among age group 20-25 and multiple infection maximum takes place between age group 45-50. These results are consistent with other findings where HPV were found to be among the most frequent types infection worldwide in women with normal cytological findings. Many studies have reported an increase in HPV infections in women 60 years of age and older. There were insufficient cases to confirm that trend in odissa. The age based study also found that maximum HPV infections were found between age 40-45.

7. Conclusion

The results from our study suggest that the distribution of HPV infection types in Odissa is in accordance with what has in other states. These data provide a baseline of infection prevalence in an unvaccinated population in Odissa. In addition, the use of data linkage provides a proof of concept for the risk factors associated with cervical cancer occurance.

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