CORRELATION BETWEEN THE HUMAN PAPILLOMAVIRUS TYPE DISTRIBUTION IN MALIGNANT AND PREMALIGNANT CERVICAL LESIONS AT THE UNIVERSITY OF BENIN TEACHING HOSPITAL

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ABSTRACT

BACKGROUND

Cervical cancer is a preventable disease and has continued to constitute a major public health problem. Persistent infection with high risk human papillomavirus (HPV) types is said to play a major role in the causation of the disease. Although, epidemiological studies have established HPV infection as the central cause of invasive cervical cancer (ICC) and its precursor lesions, only a fraction of premalignant lesions progress to ICC. It is important to know whether the HPV type distribution in premalignant lesions is representative of those that go on to cause cancer. This may help in planning more aggressive treatment modalities and more effective follow up measures for premalignant lesions when such virulent HPV types are detected. It may as well help in the evaluation of the potential impact of both existing and future prophylactic HPV vaccines.

AIM

To compare the type distribution of high risk HPVs in women with malignant and premalignant cervical lesions in the University of Benin Teaching Hospital (UBTH).

METHODS

In this case controlled study, sixty women with histologically confirmed ICC and sixty controls with histologically diagnosed cervical intraepithelial lesions (CINs), awaiting treatment at the UBTH were recruited for the study. These had cervical swabs taken for HPV testing using COBAS 4800. All collected specimens were transported to a central laboratory at Access to Basic Medical Care (ABC) foundation, Ibadan, for assay. Data analysis was done using the Statistical Package for Social Students (SPSS) version 20. Relationship between variables was assessed using Chi square test or Fisher exact test where appropriate. Pearson's correlation was used to determine the relationship between HPV types in premalignant and malignant lesions and significant differences between means was determined using Student *t* test. The level of significance was set as $p<0.05$.

RESULTS

120 subjects who met the inclusion criteria participated in the study: 60 subjects with malignant cervical lesions (ICC) and 60 controls with premalignant cervical lesions (CIN I, CIN II and CIN III). Of the sixty controls, 25 had CIN III, 19 had CIN II while 16 had CIN I. While ninety percent (54) of the 60 subjects with invasive cervical cancer tested positive to at least one hrHPV genotype, only sixty-five percent (39) of the 60 controls with premalignant lesions (i.e. 80%, 57.9% and 50% of those with CIN III, CIN II and CIN I respectively) tested positive to hr HPV testing. This too was statistically significant (*p=0.001*). While HPV-16 is responsible for 63% of the malignant lesions, it is only responsible for 25.6% of their premalignant counterparts. This was statistically significant (*p=0.001*). HPV-16 was more likely to be found in malignant than premalignant cervical lesion (*OR=4.93, 95%*

CI=1.99-12.20, p=0.001). HPV-18 was less likely to be found in malignant compared to premalignant cervical lesions. However, this association was not statistically significant (*OR=0.32, 95% CI =0.08-1.38, p=0.158*). Other hrHPV types were also less likely to be found in malignant compared to premalignant cervical lesions. This was statistically significant (*OR=0.32, 95% CI= 0.14-0.75, p=0.011*).

CONCLUSION

This study has established the fact that the hrHPV genotypes in malignant cervical lesions do not differ significantly from those in premalignant cervical lesions, but the proportion of the genotypes in individual lesions may vary. HPV-16 and -18 account for about 70% of malignant cervical lesions and nearly 50% of premalignant cervical lesions, and as such, premalignant lesions infected with these genotypes require a more aggressive management and/or closer surveillance. However, a larger study with HPV detection methods capable of detecting the other high risk HPVs individually should be carried out to explore the potential effects of the other high risk HPVs on cervical lesions in our environment.

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection worldwide with majority of individuals who engage in sexual activity becoming infected at sometime in their lifetime[i]. HPVs are small, double stranded DNA viruses that generally infect cutaneous and epithelial tissues of the anogenital tract[ii, iii]. There are around 100 types of HPV with different variations in their genetic and oncogenic potentials[iv, v]. Of these, more than 40 distinct HPV types are known to infect the genital tract and epidemiological studies to date suggest that at least 14 of these, called oncogenic or high-grade types, are significantly associated with progression to invasive cervical cancer[vi]. Persistent infection with the oncogenic HPV types has been identified by overwhelming evidence[vii, viii, ix], as necessary cause of the development of invasive cervical cancer. In 2009, the international agency for research on cancer (IARC) concluded that the types of HPV found most frequently in cervical cancer (16, 18, 31, 33, 35, 45, 52 and 58) and 4 types less frequently found (39, 51, 56 and 59) were classified as having sufficient evidence for causal relationship with cervical cancer[x]. HPV 68 was classified as probably carcinogenic[xi]. Most of these high-risk HPV (hr-HPV) types are phylogenetically related to either HPV 16 (31, 33, 35, 52 and 58) or HPV 18 (39, 45, 59 and 68)[xii]. Of these, HPV 16 and 18 alone account for up to 72% of cervical cancers[xiii]. Low risk HPVs, principally HPV 6 and 11 are predominantly involved in the development of genital warts[xiv]. These infections are generally self limiting and do not lead to malignancy[3,5].

Worldwide 530,000 women are diagnosed and 275,000 women die from cervical cancer each year and 88% of these deaths occur in developing countries[xv], including Nigeria. During the last decade, Papanicolaou (Pap) smear screening programmes significantly reduced the incidence of cervical cancer, achieving reductions in cervical cancer incidence of up to 80% in most industrialized countries where it is practised effectively[xvi, xvii]. The central concept of this exceptionally successful cancer prevention is the identification and treatment of women with high-grade cervical intraepithelial lesions (HSIL) – cervical intraepithelial neoplasia-2 and 3 (CIN2/3)[16]. Although, the Pap smear is still the undisputed screening test in most programmes to prevent cervical cancer, numerous studies could demonstrate that the sensitivity of a single Pap smear for CIN 2/3 is much lower than previously conceived[16]. There is now ample evidence that infection with hr-HPVs is a requisite intermediate step for the development of cervical cancer and its precursors[xviii]. On this basis, it has been proposed

that testing for the presence of hr-HPV could improve cervical cancer screening[18]. In a meta-analysis that included 6 different controlled studies with more than 60,000 women attending for primary cervical cancer screening, only 53% of high-grade lesions were detected by cytology compared to a sensitivity of 96% of HPV DNA testing[xix]. In most industrialized countries, screening for cervical cancer already changed from a sole conventional Pap smear-based programme to liquid-based cytology (LBC) screening followed by HPV testing for triage of borderline findings[16]. Some industrialized countries have now adopted HPV testing as a primary screening method for cervical cancer[16]. Most developing countries on the other hand lack standard screening programme resulting in most screening being opportunistic. HPV testing has yet to gain popularity in the developing world.

Until recently, conventional Pap smear was the most widely used cervical screening test. Despite the fact that it has substantially reduced the incidence and mortality of cervical cancer in well organized screening programmes, the accuracy of cytology is variable[xx]. Its sensitivity to pick up high-grade lesions varies between 50-70%[19]. Because of this variation in the quality of Pap smear and its potential to influence the detection of high-grade CIN, LBC was introduced[20]. The advantage of LBC is the improved specimen quality, the reduced reading time and availability of specimen for HPV testing[20]. However, LBC is not more sensitive for detecting high-grade CIN than conventional smear[xxi, xxii, xxiii]. In search for a more sensitive screening technique, hr-HPV screening has been proposed[20]. This has stimulated researchers to set up a number of large trials in which hr-HPV either alone or in combination with cytology has been tested against conventional or liquid based cytology[20]. The results of those trials show that overall; hr-HPV testing is about 30% more sensitive than cytology in detecting underlying or incipient CIN2+ and about 22% more sensitive in detecting CIN3+[20, xxiv]. However, the specificity of hr-HPV testing is 4-6% lower than that of cytology[24, xxv]. Besides the high sensitivity for CIN2/3, the extra-ordinarily high negative predictive value is another advantage of HPV testing[16]. Because of the very high sensitivity of HPV testing, co-testing with Pap smear was found not to be better than HPV screening alone in detecting CIN2+ lesions[xxvi]. Thus, a negative HPV test provides a better protection against cervical cancer than a negative cytological smear[20]. Moreover, HPV negative women cannot develop cervical cancer within the next 5-7 years even if they get infected the next day because the minimum latency from infection to cancer is in the range of 7-8 years[25].

It is suggested that primary HPV screening followed by cytology in all HPV positive cases will be an attractive concept in the future and that primary HPV testing at present will be cost effective in organized programmes with an extension of screening to 5-7 years[16]. Although, epidemiological studies have established HPV infection as the central cause of ICC and its precursor lesions[9], only a fraction of premalignant lesions progress to ICC. A strong candidate factor for differential progression is HPV type[xxvii]. Identifying HPV types that preferentially progress from HSIL to ICC has implications not only for follow-up protocols in ICC screening programmes, but also for prophylactic type-specific HPV vaccine trials. For ethical reasons, final outcome measures in such trials will be the prevention of HSIL. However, it is important to know whether the HPV type distribution in HSIL is representative of those that go on to cause cancer[xxviii]. This knowledge may help in planning more aggressive treatment modalities and more effective follow up measures for women with premalignant lesions in whom hr-HPV types established to preferentially progress to ICC have been detected. It may as well help in proper evaluation of the potential impact of both existing and future prophylactic HPV vaccines.

The aim of this study is to find out if the HPV types found in premalignant cervical lesions in the UBTH is representative of those prevalent in invasive cervical cancers. This is the first study involving HPV testing and specifically considering the HPV type distribution in this centre in women with malignant and premalignant cervical lesions. It will help in planning more aggressive treatment modalities and more effective follow up measures for women with premalignant lesions in whom HPV types established to preferentially progress to ICC have been detected. It will also help in proper evaluation of the potential impact of both existing and future prophylactic HPV vaccines in this centre.

METHODOLOGY

STUDY SITE

This study was conducted at the Obstetrics and Gynaecology Department of the University of Benin Teaching Hospital, Benin City. The University of Benin Teaching Hospital serves as a major referral centre for Edo, Delta, Kogi and Ondo States. Patients are usually referred from general hospitals, government owned health centres, private Hospitals and from other departments in the hospital.

STUDY DESIGN

It was a case-controlled study among women with histologically confirmed invasive cervical cancer awaiting treatment (cases) and women with histologically diagnosed premalignant cervical lesions (CIN 1, 2 and 3) awaiting treatment (controls).

ETHICAL CONSIDERATION

Ethical approval for this work was obtained from the Research and Ethics Committee of the University of Benin Teaching Hospital. All the patients were counselled about the study and a written consent was obtained from each patient.

DATA ANALYSIS

Data analysis was done using the IBM Statistical Package for Social Students for Windows version 20 (IBM SPSS 20). Categorical variables were expressed as absolute numbers and percentages and significant differences were determined using the Chi square test or Fisher exact test where appropriate. Pearson's correlation was used to obtain the correlation coefficient. The level of significance was set as $p<0.05$.

RESULTS

One hundred and twenty subjects who met the inclusion criteria participated in the study: 60 subjects with malignant cervical lesions (ICC) and 60 controls with premalignant cervical lesions (CIN I, CIN II and CIN III). Of the sixty controls, 25 had CIN III, nineteen had CIN II while 16 had CIN I. Of the 120 subjects recruited overall, only thirty-nine (32.5%) had a prior cervical cancer screening. None of the subjects with invasive cervical cancer had a prior screening.

Table 1: Socio-demographic characteristics of subjects and C ervical lesions

Characteristic	CIN1	CIN2	CIN3	ICC	P. value
	Freq (%)	Freq (%)	Freq (%)	Freq (%)	
Age (years)					
25 – 34	0 (0)	0 (0)	0 (0)	12 (20.0)	
35 – 44	10 (62.5)	2 (10.5)	5 (20.0)	1 (1.7)	
45 – 54	2 (12.5)	14 (73.7)	20 (80.0)	12 (20.0)	**0.020**
55 – 64	4 (25.5)	3 (15.8)	0 (0)	26 (43.3)	
≥65	0 (0)	0 (0)	0 (0)	9 (15.0)	
Parity					
0	6 (37.5)	0 (0)	0 (0)	0 (0)	
1-4	6 (37.5)	9 (47.4)	19 (76.0)	25 (41.7)	**<0.001**
≥5	4 (25.0)	10 (52.6)	6 (24.0)	35 (58.3)	
Social Class					
1-2	5 (50.0)	9 (47.4)	19 (76.0)	10 (16.7)	
3	2 (20.0)	3 (15.8)	0 (0)	2 (3.3)	<**0.001**
4-5	3 (30.0)	7 (36.8)	6 (24.0)	48 (80.0)	
Marital Status					
Single	6 (37.5)	0 (0)	0 (0)	0 (0)	
Married	10 (62.5)	19 (100.0)	25 (100.0)	60 (100.0)	<**0.001**

Table 1 shows the relationship between the socio-demographic characteristics of subjects and cervical lesions.

There was no subject in the age group below 25 years. The mean age of the subjects was 51.41±8.69 years (minimum=31 years, maximum=65 years). Whereas no premalignant lesion (CIN I-III) occurred in subjects 65 years or older, all the premalignant cervical lesions occurred in subjects between 35 and 64+ years. Over three-quarters of high grade lesions (CIN II and III) occurred in subjects between 45 and 54 years. Nearly, 80% of ICC cases occurred in subjects 45 years or older. These findings though, were not statistically significant (*p=0.020*).

Although 37.5% of low grade (CIN I) lesions occurred in nulliparous subjects, all high grade and malignant lesions occurred in parous subjects. This was statistically significant (p=<0.001). While the social class of subjects did not appear to have a definite relationship with premalignant cervical lesions, 80% of the malignant lesions occurred in subjects of low social class (status 4-5). This was statistically significant (*p=<0.001*).
While no malignant or high grade lesions occurred in the subjects who were single, all the high grade and malignant lesions occurred in subjects who were married. This was also statistically significant (*p=<0.001*).

Table 2: Cervical lesions and HPV DNA Testing

HPV Test	CIN1 N (%)	CIN2 N (%)	CIN3 N (%)	ICC N (%)	P. value
Positive	8 (50.0)	11 (57.9)	20 (80.0)	54 (90.0)	
Negative	8 (50.0)	8 (42.1)	5 (20.0)	6 (10.0)	**0.001**
Total	16 (100)	19 (100)	25 (100)	60 (100)	

Table 2 relates the various cervical lesions with HPV DNA testing.

While ninety percent (54) of the sixty subjects with invasive cervical cancer tested positive to at least one high risk types of the human papillomavirus, only sixty-five percent (39) of the sixty controls with premalignant lesions (i.e. 80%, 57.9% and 50% of those with CIN III, CIN II and CIN I respectively) tested positive to hr HPV testing. This too was statistically significant (*p=0.001*).

Table 3: HPV type distribution in various cervical lesions

HPV type	**CIN1**	**CIN2**	**CIN3**	**ICC**	**P. value**
	N (%)	**N (%)**	**N (%)**	**N (%)**	
16	2 (25.0)	2 (18.2)	6 (30.0)	34 (63.0)	
18	0 (0)	0 (0)	6 (30.0)	3 (5.5)	<**0.001**
*Others	6 (75.0)	9 (81.8)	8 (40.0)	17 (31.5)	

**hrHPV types- 31, 33, 35, 39, 45, 51, 52, 56, 58, 66, and 68*

Table 3 shows the human papillomavirus type distribution in the various cervical lesions.

While HPV-16 was detected in 63% of HPV positive invasive cervical cancers in this study, it was detected in just 30%, 18.2% and 25% of HPV positive CIN III, CIN II and CIN I respectively. Other high risk HPV types (one or more of HPV -31, 33, 35, 45, 51, 52, 56, 58, 66 and 68) were detected in over 75% of CIN I and CIN II. HPV -18 was only detected in 5.5% of HPV positive ICC cases. These findings were of statistical significance (*p=<0.001*).

Table 4: HPV type distribution in various cervical lesions and Parity of subjects

HPV type	**Parity**											
	0				**1 – 4**				**≥ 5**			
	CIN1	**CIN2**	**CIN3**	**ICC**	**CIN1**	**CIN2**	**CIN3**	**ICC**	**CIN1**	**CIN2**	**CIN3**	**ICC**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
16	0 (0)	-	-	-	2 (100)	0 (0)	0 (0)	13(65.0)	-	2 (100)	6 (100)	21(61.8)
18	0 (0)	-	-	-	0 (0)	0 (0)	6(42.9)	1 (5.0)	-	0 (0)	0 (0)	2 (5.9)
***Others**	6 (100)	-	-	-	0 (0)	9 (100)	8(57.1)	6 (30.0)	-	0 (0)	0 (0)	11 (32.3)
P. value		-					**<0.001**				**0.351**	

*N=number, %= percent, *HPV types- 31, 33, 35, 39, 45, 51, 52, 56, 58, 66, and 68*

Table 4 shows the HPV type distribution in various cervical lesions across parities.

Other hr HPV types (than HPV-16 and 18) accounted for the six cases of HPV positive CIN I lesions among nulliparous subjects. While all the HPV positive high grade lesions in the grandmultiparous subjects were caused by HPV-16, only about 62% of all the HPV positive ICC cases in the same group of subjects were caused by HPV-16. This however, did not achieve statistical significance (*p=0.351*).

Table 5: HPV type distribution in various cervical lesions and Social class of Patients

HPV type	**Social Class**											
	1 – 2				**3**				**4 – 5**			
	CIN1	**CIN2**	**CIN3**	**ICC**	**CIN1**	**CIN2**	**CIN3**	**ICC**	**CIN1**	**CIN2**	**CIN3**	**ICC**
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
16	-	0 (0)	0 (0)	7 (87.5)	2 (100)	-	-	0 (0)	-	2 (100)	6 (100)	27 (61.4)
18	-	0 (0)	6 (42.9)	1 (12.5)	0 (0)	-	-	0 (0)	-	0 (0)	0 (0)	2 (4.5)
*Others	-	9 (100)	8 (57.1)	0 (0)	0 (0)	-	-	2 (100)	-	0 (0)	0 (0)	15 (34.1)
P.value			**<0.001**				**0.046**				**0.332**	

*N=number, %= percent, *hrHPV types- 31, 33, 35, 39, 45, 51, 52, 56, 58, 66, and 68*

Table 5 shows the HPV type distribution in various cervical lesions across various social classes.

Of the 8 HPV positive ICC subjects in the high social class, seven (87.5%) were caused by HPV-16, the remainder was caused by HPV-18. This is statistically significant (*p=<0.001*).

In the low social class group where forty-four ICC cases were HPV positive, only 27 (about 61 percent) were caused by HPV-16. This did not attain statistical significance (*p=0.332*).

Of the 60 cases of invasive cervical cancer recruited, fifty-four (90%) were squamous cell carcinoma (SCC) of various grades while 6 (ten percent) were adnocarcinoma. While fifty-one (94%) of the 54 SCC cases tested positive for hrHPV DNA, only 3 (fifty percent) of the adenocarcinoma cases were positive for hrHPV DNA. Whereas all the three hrHPV positive adenocarcinoma cases were caused by HPV-18, only thirty-four (67%) of the 51 hrHPV positive SCC cases were caused by HPV-16, the remaining seventeen (33%) were caused by other hrHPV types.

Table 6: HPV types and Premalinant versus Malignant Cervical lesion

HPV genotype	Cervical Lesion				OR	95% CI		P value
	Premalignant		Malignant					
	N	%	N	%				
HPV-16	10	25.6%	34	63.0%	4.93	1.99	12.20	0.001
HPV-18	6	15.4%	3	5.6%	0.32	0.08	1.38	0.158
Others	23	59.0%	17	31.5%	0.32	0.14	0.75	0.011

*N=number, %= percent, *hrHPV types- 31, 33, 35, 39, 45, 51, 52, 56, 58, 66, and 68*

Table 6 shows the comparison of the likelihood of HPV genotypes between malignant and premalignant cervical lesions.

While HPV-16 was responsible for 63% of the malignant lesions, it was only responsible for 25.6% of their premalignant counterparts. This was statistically significant (*p=0.001*). HPV-16 was more likely to be found in malignant than premalignant cervical lesion (*OR=4.93, 95% CI=1.99-12.20, p=0.001*). HPV-18 was less likely to be found in malignant compared to premalignant cervical lesions. However, this association was not statistically significant (*OR=0.32, 95% CI =0.08-1.38, p=0.158*). Other hrHPV types were also less likely to be found in malignant compared to premalignant cervical lesions. This was statistically significant (*OR=0.32, 95% CI= 0.14-0.75, p=0.011*).

DISCUSSION

This study found hrHPV prevalence of 90.0% in malignant cervical lesions (ICC) compared to 65% in premalignant lesions, although the prevalence of hrHPV in CIN III (80.0%) was higher compared to CIN I (50%). This is comparable to the findings of other studies[28, 29-31]. In a recent study in India, Srivastava *et al*[31] found hrHPV prevalences of 73.3% and 95.8% in CINs and ICC cases respectively, while Abd El-Azim *et al*[30] in Egypt found hrHPV prevalence of 85.7% and 93.3% in CIN2/3 and CC cases respectively. These all fell short of the findings of hrHPV prevalence of 99.7% by Walboomers *et al*[9]. This difference has been attributed to inadequate sampling and possibly, hrHPV detection methods used[9].

All the high risk HPV types were detected in both malignant and premalignt lesion, although other high risk HPV types than HPV-16 and -18 (including types 31, 33, 35, 39, 45, 51, 52, 56, 58, 66, and 68) were lumped together in one pool. HPV-16 alone accounted for 63.0% of

ICC and 25.6% of the premalignant lesions. Overall, HPV-16 and -18 were found in 68.6% of ICC and 41.0% of the premalignant lesions. This is similar to the findings of Clifford and colleagues[28]. In that study, the prevalences of HPV-16 and -18 combined were 70% and 50% in SCC and HSIL respectively. In the study by Abd El-Azim *et al*[30], the prevalences of HPV -16 and 18 combined were 80% and 60% in ICC and CIN2/3 respectively. This is higher than that obtained in this study and probably reflects the geographical variation in HPV type distribution[75]. These prevalences in the work of Srivastava *et al*[31] stood at 52% and 27% for malignant and premalignant cervical lesions respectively. These were lower than those of this study and probably reflect the same geographical differences in HPV type distribution worldwide.

In this study, HPV-16 was more likely to be found in malignant than premalignant cervical lesions. This implies that premalignant lesions with HPV -16 infections are more likely to progress to malignancy than those lacking HPV-16 infection. Patients with such lesions should therefore be offered more aggressive treatment and follow-up. Conversely, both HPV-18 and other hrHPVs were less likely to be found in malignant than in premalignant cervical lesions. However, whereas this association was weak for HPV-18, it was strong for the other hrHPVs. These findings are in agreement with those of Clifford and colleagues who suggested that HSIL infected with HPV16, 18 or 45 are more likely to progress to SCC than HSIL infected with other HR types. They further recommended that HSIL infected with HPV16, 18 or 45 are more likely to progress to SCC than HSIL infected with other HR types. The finding of a noticeable absence of HPV-45 in the HSIL group by Smith and co-workers[29], has made HPV-16 and -18 the undisputable cofactor for selective progression from premalignant to malignant cervical lesions. However, the method of testing for HPV used in this study, in which all other high risk HPVs excepting HPV-16 and -18 were lumped together in a single pool, did not provide the chance to test for HPV-45 in this study population.

This study observed that only 32.5% of the study population had a prior cervical cancer screening, confirming opportunistic nature of screening in our part of the world and dire lack of standard screening programme for this preventable disease. Also, none of the subjects with ICC had a prior screening for cervical cancer. This was a fall out of the same prevailing lack of an organized screening programme.

In this study, we observed that while parity, social class and marital status of subjects correlated well with malignant cervical lesions, age did not appear to correlate as well with the disease. All the malignant and high grade lesions occurred in the married, parous subjects and 80% of the malignant lesions were in subjects of low social class. It is no coincidence that these factors are direct or indirect risk factors for cervical cancer. In general, socio-demographic characteristics did not appear to influence HPV type distribution on cervical lesions. This is understandable since the source of HPV infection rather than these characteristics determine the type of the virus transmitted.

This study has established the fact that the hrHPV genotypes in malignant cervical lesions do not differ significantly from those in premalignant cervical lesions however, the proportion of these HPV genotypes in individual lesions may vary. HPV-16 and -18 account for about 70% of malignant cervical lesions and nearly 50% of premalignant cervical lesions, and as such, premalignant lesions infected with these genotypes require a more aggressive management and/or closer surveillance. However, a larger study with HPV detection methods capable of detecting the other high risk HPVs singularly should be carried out to explore the potential

effects of the other high risk HPVs on cervical lesions in our environment so as to come up with more robust conclusion.

CONCLUSION AND RECOMMENDATIONS

Persistent infection with high risk human papillomavirus has been demonstrated as the undisputable aetiological factor in the causation of cervical cancer. Various studies have profiled the type distribution of the high risk HPV in cervical lesions across various populations. Although there appears to be subtle differences in HPV type distribution in malignant and premalignant lesions across geographical locations, a major consistent finding in all the studies is the fact that over 2/3 of the ICC cases and about half of the premalignant lesions are accounted for by HPV-16 and-18 with only minor differences observed in the distribution of the other less common high risk HPV types.

This fact was established by this study. Thus the hrHPV genotypes in malignant cervical lesions do not differ significantly from those in premalignant cervical lesions. Since HPV-16 and -18 account for about 70% of malignant cervical lesions and nearly 50% of premalignant cervical lesions, premalignant lesions infected with these genotypes may require a more aggressive management and/or closer surveillance. However, a larger study with HPV detection methods capable of detecting the other high risk HPVs singularly should be carried out to explore the potential effects of the other high risk HPVs on cervical lesions in this environment so as to come up with more robust conclusion.

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