

LETTER TO THE EDITOR

Dear Sir,

Human papillomavirus types 52 and 58 are prevalent in cervical cancer from Chinese women

Huang et al. (1997) have reported in this journal that human papillomavirus (HPV) types 52 and 58 were the most common types in tumor tissues obtained from Chinese women diagnosed with invasive cervical cancer in Shanghai. Fifteen (48%) of the 31 HPV-positive specimens from women diagnosed with cervical squamous-cell carcinoma were positive for HPV types 52 and/or 58 (HPV 52/58), while 13 (42%) contained the so-called major oncogenic types 16 and/or 18. These results are consistent with our previous report (Liaw et al., 1995). In our case-control study in Taiwan, among those who were HPV positive, the combined prevalence of HPV 52/58 was 39% among women diagnosed with high-grade squamous intraepithelial lesions (HSIL), second only to that of HPV 16 (48%). Moreover, among those who were HPV positive, HPV types 52 and 58 combined were the most common types among those diagnosed with low-grade squamous intra-epithelial lesions (LSIL) (29%) and among the women with normal cervical cytology (38%).

Additional data from our expanded case-control study provide further support that HPV 52 and 58 are frequently found among HPV-positive Chinese women. Details of our original case-control study have been described elsewhere (Liaw et al., 1995). In the expanded series, in addition to the original 88 pathologically confirmed cases (40 with LSIL and 48 with HSIL) and 261 cytologically normal controls, 62 new pathologically confirmed cases and 159 controls were added. Altogether, 150 cases (including 51 with LSIL, 91 with HSIL, and 8 with invasive cancer) and 420 controls were included in the expanded study. Because of the small number of invasive cancer cases, women diagnosed with invasive cancer were grouped with those with HSIL. Cervical cells were obtained from cases and controls and assayed by a polymerase chain reaction (PCR)-based method for detection of HPV DNA (Manos et al., 1989). The amplification reactions included the modified L1 consensus primer pair MY09 and MY11. Amplification products were hybridized with a generic probe to determine HPV positivity and with specific oligonucleotide probes to identify individual types, including 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 57, 58, 59, 66, 68, PAP155, PAP238A, PAP291 and W13B. Of the 570 cervical samples, all but 9 samples, for which there was insufficient material, were tested successfully for HPV DNA.

The overall prevalences of HPV infection were 10%, 59% and 81% among controls, LSIL cases and HSIL cases, respectively (data not shown). As shown in Table I, among those who were HPV positive, infection with HPV 52/58 was common in controls (27.5% of the HPV-positive cases), LSIL (20%) and HSIL (31.3%) cases. Among the cytologically normal controls and LSIL cases, HPV 52/58 was the most common type, while

HPV 16 was found in only 7.5% of the HPV-positive controls and 16.7% of the HPV-positive LSIL cases. In addition, after HPV 16 (47.5% of the HPV-positive cases), HPV type 52/58 was the second most common type found among the HPV-positive HSIL cases.

Based on our data, the proportion of infection with HPV 52/58 was high among HPV-positive women with LSIL and women with HSIL. Coupled with the findings of high prevalence of these 2 HPV types in cervical cancer patients reported by Huang et al. (1997) the data suggest that HPV 52/58 is prevalent across the full spectrum of cervical neoplasia in Chinese women. However, different results have been reported from an international study testing approximately 1,000 tumor tissue samples from cervical cancer patients from 22 countries, using the same PCR-based method that was employed in our study (Bosch et al., 1995). In the international study, the prevalence of HPV 52/58 was low (0–3%), compared with the 40–65% prevalence of HPV 16, with little geographic variation. Reasons for the discrepancy between the international study and the 2 studies among Chinese women are not clear, perhaps because few Chinese women were included in the international study.

In the studies of Huang et al. (1997) and Bosch et al. (1995), HPV was tested in tumor tissues from women with invasive cervical cancer only, while we examined HPV DNA in cervical cells not only from the women with cervical neoplasia but also from those with normal cytology. In our study, HPV 16 was common only among women with cervical neoplasia, while HPV 52/58 was prevalent among women with either cervical neoplasia or normal cytology. Therefore, the odds ratios (ORs) associated with HPV 52/58 were much smaller than those for HPV 16. Specifically, the ORs associated with HPV 52/58 infection for LSIL and HSIL were 12 [95% confidence interval (CI) 4–38] and 42 (95% CI 17–105), respectively, while the ORs associated with HPV type 16 were much higher (OR = 29, 95% CI 6–139 for LSIL; OR = 326, 95% CI 90–1,186 for HSIL).

Despite the lower ORs associated with HPV 52/58, these 2 types of HPV account for a substantial proportion of cervical neoplasia in Taiwan, because the proportion of cases attributable to a specific HPV type depends not only on the magnitude of the risk (ORs) but also on the prevalence of that HPV type. In our study, while HPV 16 accounts for 9% of LSIL and 38% of HSIL, HPV 52/58 accounts for a substantial 11% of LSIL and 25% of HSIL. The impact of infection with HPV 52/58 in Chinese women may be as important as that of HPV 16, due to the high prevalence of these HPV types in the population. The role of infection with HPV 52/58 in other populations is unclear and warrants further investigation, since high prevalence of

TABLE I – PERCENTAGE OF HPV INFECTION WITH SELECTED TYPES AMONG HPV-POSITIVE STUDY SUBJECTS (TAIWAN, 1991–1993)

HPV type	Controls (n = 420)		LSIL (n = 51)		HSIL + cancer (n = 99)	
	Number	% ¹	Number	% ¹	Number	% ¹
All HPV	40	100	30	100	80	100
HPV 16	3	7.5	5	16.7	38	47.5
HPV 18	1	2.5	4	13.3	4	5.0
HPV 52	6	15.0	5	16.7	13	16.3
HPV 58	5	12.5	1	3.3	13	16.3
HPV 52/58	11	27.5	6	20.0	25 ²	31.3

¹Percentage among the HPV-positive subjects only. ²One HSIL case had infections with both HPV 52 and 58.

HPV 52/58 has been found in women with both cervical neoplasia and normal cytology in an ongoing study in Costa Rica (R. Herrero, personal communication).

In conclusion, most of the previous studies investigating the role of HPV infection in cervical cancer etiology included only the “main” cancer-associated types, mostly HPV 16, 18 and 33 (IARC monograph 1995). Although HPV 52 and 58 are phyloge-

netically close and both belong to the HPV 16 group, their importance has seldom been evaluated. Future studies need to incorporate probes for a wide range of HPV types to evaluate the role of HPV 52/58, and perhaps other types, in studying the etiology of cervical neoplasia.

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