Role of human papillomavirus in cancers

To the Editor: With my interest piqued, I read the article in *SAMJ* by Maroga *et al*. on the 'Profile of human papillomavirus genotypes in breast and oesophageal cancer patients in Pretoria, South Africa.'[1] Studies such as these are essential in investigating the causative factors associated with cancers, especially in our region, where more data are required to inform us on the epidemiology of cancers. However, the role of human papillomavirus (HPV) in breast cancer and oesophageal cancer is not clearly established. This is in contrast to cervical cancer, anal cancer, penile cancer, vaginal cancer, vulvar cancer and oropharyngeal cancer, in which there is proven causation by HPV.[2]

HPV is ubiquitous, with infections found worldwide. The presence of HPV DNA alone could be coincidental and not directly related to the cancer, or it could be a co-factor. Transcriptionally active HPV in the form of HPV E6/E7 mRNA detection is the gold standard for clinically relevant oncogenic HPV.[3] It would have been valuable if other methods were employed in the study, such as p16 immunohistochemistry, HPV E6/E7 mRNA or RNA *in situ* hybridisation. This would add more strength to the findings. However, many of these methods are HPV type-specific, commonly targeting HPV16 and HPV18, and this study detected a wide range of other high-risk HPV types. The significance of these findings and the high prevalence of HPV co-infection are interesting to explore further.

HPV16 is most frequently associated with HPV-related cancers globally.[4] In the study, it is noteworthy that other high-risk HPV types were more common or as frequently found as HPV16. In particular, HPV70 and HPV82, which were frequently detected in the study, are classified as group 2b carcinogens (possibly carcinogenic), compared with HPV16 and HPV51, which are group 1 carcinogens.[5] Most studies from South Africa (SA) on HPV genotype distribution in cervical cancers found that HPV16 was predominant.[6-9] There was also detection of a substantial proportion of other high-risk HPV types, including HPV18, 33, 35, 39, 45 and 56, as well as infection with multiple high-risk HPV types.[6-9] Lebelo *et al*.[8] showed that there were higher HPV16 viral loads in cervical cancers with co-infections, suggesting HPV16 as the cancer driver.

Safe and effective vaccines are available for prevention of HPV. Besides the use of the bivalent vaccine in the school-based programme targeting young girls before exposure to HPV, studies have shown benefits in catch-up vaccination in older age groups as well as vaccinating males.[10] Although there is some cross-protection with the bivalent vaccine, use of the nonavalent vaccine, which covers HPV6, 11, 16, 18, 31, 33, 45, 52 and 58 has been modelled, to be cost-effective in SA.[11] The burden of genital warts and recurrent respiratory papillomatosis in SA necessitates the need to include HPV6 and 11. Mbulawa *et al*.[9] highlighted the role of HPV35 in cervical intraepithelial neoplasia and cancer in SA, which is not covered by the current vaccines.

Optimal HPV vaccine coverage and widespread implementation of HPV testing into our cervical cancer screening programme must be our priority to reduce HPV-related diseases.

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