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BRIEF REPORT

The prevalence of human papillomavirus infection in Mombasa, Kenya

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Abstract
Objectives A human papillomavirus (HPV) prevalence survey was done in Mombasa, Kenya, to improve the knowledge of HPV prevalence and genotype distribution in sub-Saharan African countries overall, and in women of different ages.
Methods HPV prevalence was assessed using PCR in women older than 15 years attending family planning and mother–child care services.
Results Among 496 women, HPV prevalence was high (42.3%; 95% CI: 37.9–46.8; world age-standardized). Moreover, 46% of HPV-positive women harbored multiple-type infections. The most common types were HPV58 (10.5% of women), HPV16 (7.7%), HPV53 (6.7%), HPV18 (4.6%), and HPV6 (4.4%), and the prevalence of any high-risk HPV type was 28.8%. HPV prevalence was elevated among all age-groups (range 36.4–45.7%). Independent associations with HPV positivity were found for being in a polygamous marriage (OR = 1.7) and lifetime number of sexual partners (OR for ≥3 vs. 1 = 1.5), although they were of only borderline statistical significance.
Conclusions These findings differ from other world regions, showing a high HPV burden in all age-groups with a high proportion of multiple-type infections. Our data strengthen the urgency of HPV vaccination in Kenya but also highlight the elevated number of women who would have positive results in an HPV-based screening program in the country.

Keywords Cervical cancer · Human papillomavirus prevalence · Kenya · Africa

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Introduction

Sub-Saharan African countries are among those with the highest incidence of cervical cancer [1] and the highest population-based human papillomavirus (HPV) prevalence worldwide [2, 3]. It is also the region with the highest prevalence of HIV, an infection that worsens the course of HPV infection and hence increases cervical cancer risk [4].

Prevention of cervical cancer in this region through the widely adopted Pap smear method or alternative visual inspection techniques has been challenging [5], but new prevention options such as HPV screening and HPV vaccination are being evaluated and may be a way forward. However, the epidemiology of HPV is not well described

yet in many African countries [6]; hence, the aim of this study was to describe the prevalence of cervical HPV in a coastal district of Kenya.

Materials and methods

Between 2002 and 2004, women over 15 years of age were recruited in an age-stratified way from family planning or mother–child health care services from nine primary health care centers throughout the Mombasa District. All participants signed informed consent forms, and the study was approved by the Kenyatta National Hospital Ethical Review Committee.

After a structured questionnaire including information on socio-demographics and sexual history was administered, cervical exfoliated cells were collected by a nurse using a cervex brush (Rovers Medical Devices, Oss, The Netherlands). The brush was smeared on a glass slide for Pap smear, after which the tip of the brush was kept in Standard Transport Medium (Qiagen, Valencia, California, USA) for HPV testing. The nurse then performed visual inspection with acetic acid (VIA), as previously described [7]. The slides and samples were transported to the Coast Provincial General Hospital (CPGH), where the Pap smear was processed and the HPV specimen was frozen at −20°C. In case of abnormal Pap smear or positive VIA, the woman was referred to the CPGH for colposcopy, and in case of a visible lesion, a biopsy was taken.

The Pap smear slides and biopsies were processed and read at the CPGH by qualified staff under supervision of the provincial pathologist (KM). Cytology was reported according to the Bethesda classification. All abnormal smears, as well as 10% of negatives and all biopsies were reviewed for quality control by a teaching pathologist at the University of Nairobi (LM). Cervical abnormalities were defined as histological cervical intraepithelial neoplasia (CIN) grade 1 or worse, or a cytological diagnosis of atypical squamous cells of undetermined significance or worse in women who failed to attend the confirmatory colposcopy/biopsy visit.

HPV samples were shipped to the Laboratory of Virology, AIDS Center "San Luigi", IRCCS Hospital San Raffaele, Milan, Italy, where HPV DNA was isolated by the Qiagen DNA mini-kit extraction method according to the manufacturer's instructions. The presence of human DNA was confirmed by beta-globin PCR analysis, and HPV DNA amplification was performed using degenerate general primers MY09/11 and GP5+/6+ and run on agarose gel to visualize positive reaction of the appropriate molecular weight. All positive samples were reamplified and typed using the Linear Arrays HPV Genotyping Test (Roche Molecular Systems, Alameda, California, USA) ($n = 177$) or the Clinical Arrays Human Papillomavirus Test (Genomica, Madrid, Spain) ($n = 31$), according to the manufacturer's instructions. The two tests detected 33 common HPV types, which are the object of the present report. HPV-positive samples that could not be typed were assigned HPV genotype X (uncharacterized type). HPV types considered high risk included HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 [8]. All others were considered low risk.

Results

Of the 534 women enrolled in the study, 17 had beta-globin-negative cervical samples and another 21 had unsatisfactory cytological results. Out of the remaining 496 women, 52 had biopsies taken following abnormal cytology or VIA results. Fifteen women had abnormal cytological results but did not undergo colposcopy/biopsy. Overall, 42 (8.5%) women had cervical abnormalities, including 22 (4.4%) CIN grade 2 or worse on biopsy or high-grade squamous intraepithelial lesions on cytology for those who did not return for the confirmatory colposcopy/biopsy visit.

The prevalence of infection with any HPV type was 41.9% (Table 1). World age-standardized overall HPV prevalence was 42.3% (95% CI: 37.9–46.8). In total, 22.6% of women had single-type infections, 19.4% had multiple-type infections, and 29 individual HPV types were identified.

The five most common types in either single- or multiple-type infections were HPV58 (10.5% of women), HPV16 (7.7%), HPV53 (6.7%), HPV18 (4.6%), and HPV6 (4.4%). High-risk HPV types were found in 28.8% of study women and much more often in women with cervical abnormalities (45.2%), compared to women without cervical abnormalities (27.3%) ($p = 0.014$).

Figure 1 shows the prevalence of HPV by oncogenic risk category and by age-group. HPV prevalence remained high in all age-groups (range: 36.4–45.7%), resulting in a 'flat' prevalence curve. Relative proportions of HPV prevalence for types 16 and/or 18, high-risk types other than 16/18, and low-risk types also did not differ significantly by age-group.

The following possible demographic or behavioral risk factors for HPV positivity were investigated: age, education level, religion, marital status, contraceptive use, being in a polygamous marriage, lifetime number and recent (last 12 months) number of sexual partners, husband's extramarital relationships, having ever been paid for sex, cigarette smoking, history of malaria, and regular use of open wood fire for cooking (data not shown). Although the results were not statistically significant, being in a polygamous marriage (OR = 1.7; 95% CI: 1.0–2.7) and lifetime number of sexual partners (OR for ≥3 vs. 1 = 1.5; 95%

Table 1 Prevalence of human papillomavirus (HPV) types by the presence of cervical abnormalities and overall among 496 women. Mombasa, Kenya, 2002–2004

	Normal cervix ($n = 454$)			Abnormal cervix ($n = 42$)			Total ($n = 496$)		
	Single	Multiple	Total (%)	Single	Multiple	Total (%)	Single	Multiple	Total (%)
Negative	–	–	271 (59.7)	–	–	17 (40.5)	–	–	288 (58.1)
Positive	94	89	183 (40.3)	18	7	25 (59.5)	112	96	208 (41.9)
High-risk HPV+	44	80	124 (27.3)	12	7	19 (45.2)	55	87	143 (28.8)
Low-risk HPV+	51	68	119 (26.2)	6	5	11 (26.2)	56	74	130 (26.2)
High-risk infections									
HPV16	13	21	34 (7.5)	3	1	4 (9.5)	16	22	38 (7.7)
HPV18	6	14	20 (4.4)	2	1	3 (7.1)	8	15	23 (4.6)
HPV31	1	7	8 (1.8)	0	1	1 (2.4)	1	8	9 (1.8)
HPV33	1	14	15 (3.3)	0	0	0 (0.0)	1	14	15 (3.0)
HPV35	0	2	2 (0.4)	0	1	1 (2.4)	0	3	3 (0.6)
HPV39	0	4	4 (0.9)	1	0	1 (2.4)	1	4	5 (1.0)
HPV45	0	8	8 (1.8)	0	3	3 (7.1)	0	11	11 (2.2)
HPV51	2	14	16 (3.5)	0	0	0 (0.0)	2	14	16 (3.2)
HPV52	3	16	19 (4.2)	1	0	1 (2.4)	4	16	20 (4.0)
HPV56	0	8	8 (1.8)	0	0	0 (0.0)	0	8	8 (1.6)
HPV58	13	32	45 (9.9)	4	3	7 (16.7)	17	35	52 (10.5)
HPV59	4	2	6 (1.3)	0	0	0 (0.0)	4	2	6 (1.2)
HPV68	0	7	7 (1.5)	1	0	1 (2.4)	1	7	8 (1.6)
HPV73	1	5	6 (1.3)	0	0	0 (0.0)	1	5	6 (1.2)
HPV82	0	2	2 (0.4)	0	0	0 (0.0)	0	2	2 (0.4)
Low-risk infections									
HPV6	4	17	21 (4.6)	1	0	1 (2.4)	5	17	22 (4.4)
HPV11	2	12	14 (3.1)	0	0	0 (0.0)	2	12	14 (2.8)
HPV42	0	5	5 (1.1)	0	0	0 (0.0)	0	5	5 (1.0)
HPV53	4	26	30 (6.6)	1	2	3 (7.1)	5	28	33 (6.7)
HPV54	1	0	1 (0.2)	0	0	0 (0.0)	1	0	1 (0.2)
HPV61	3	13	16 (3.5)	0	1	1 (2.4)	3	14	17 (3.4)
HPV62	2	7	9 (2.0)	0	0	0 (0.0)	2	7	9 (1.8)
HPV66	2	10	12 (2.6)	0	1	1 (2.4)	2	11	13 (2.6)
HPV70	0	3	3 (0.7)	0	1	1 (2.4)	0	4	4 (0.8)
HPV72	1	0	1 (0.2)	0	0	0 (0.0)	1	0	1 (0.2)
HPV74	0	2	2 (0.4)	0	0	0 (0.0)	0	2	2 (0.4)
HPV81	3	9	12 (2.6)	0	0	0 (0.0)	3	9	12 (2.4)
HPV83	2	7	9 (2.0)	0	0	0 (0.0)	2	7	9 (1.8)
HPV84	1	7	8 (1.8)	0	0	0 (0.0)	1	7	8 (1.6)
HPVX	24	0	26 (5.7)	4	0	4 (9.5)	28	1	30 (6.0)

CI: 0.9–2.6, p for trend = 0.15) could be associated with increased risk of HPV infection in a model adjusted for age, lifetime number of sexual partners, and polygamy.

Discussion

This study showed a high prevalence of HPV (42.3%, age-standardized), similar to that found in other sub-Saharan African populations in the International Agency for Research on Cancer (IARC) HPV prevalence surveys: 28.3% age-standardized prevalence in Ibadan, Nigeria [9], and 51.5% in Conakry, Guinea [10]. A previous study in Kenya showed a similar 44.3% HPV prevalence in a population of family planning attendees aged 25–55 years in Nairobi [11]. Not surprisingly for sub-Saharan Africa [9–13], we found that half of HPV-positive women were infected with multiple types.

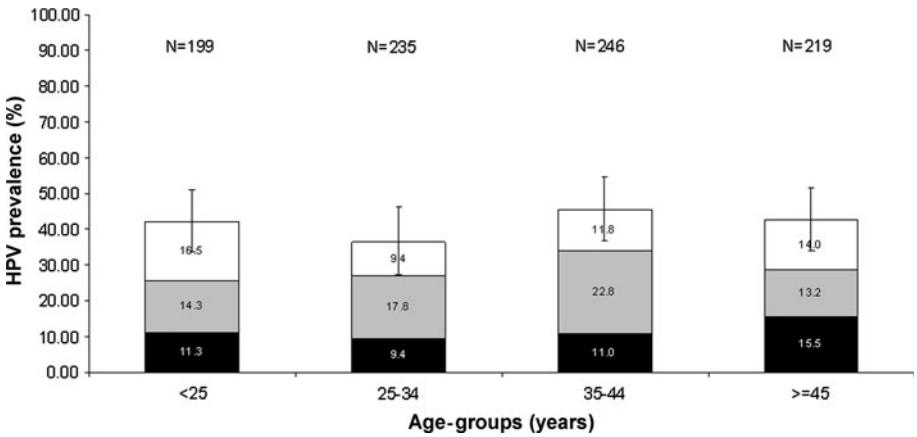

Fig. 1 Age-specific prevalence of cervical human papillomavirus (HPV) DNA by oncogenic groups among 496 women, Mombasa, Kenya, 2002–2004. *Vertical bars* indicate 95% confidence intervals of overall HPV prevalence; ■ HPV16 and/or 18, ▨ Other high-risk HPV, □ Low-risk HPV only

HPV prevalence was similarly high across all age-groups, as shown before in some low-resource regions with high cervical cancer incidence in Africa and Asia [3, 9, 10, 14–16]. This contrasts with findings from the United States and Europe, where peaks of HPV prevalence were consistently seen before the age of 25–35 years, with a steady decline thereafter [17]. However, some studies showed HPV prevalence curves that also decline with age in Zimbabwe [18, 19], Uganda [20], Kenya (Nairobi) [11], Mozambique [12], and South Africa [21]. It is not yet clear what causes these flat elevated age curves. A possible explanation is that the sexual behavior of these women and/or their partners does not change with age to the same extent as in Western countries.

Whereas HPV16 is usually the most important type detected among women with normal cytology in regions other than sub-Saharan Africa [2], the prevalence of HPV16 in our study was high, (18.6%; 34/183 HPV-positive samples), but lower than HPV58 (24.6%; 45/183).

HIV testing was not done in this study. Sentinel data, however, estimated the HIV prevalence in pregnant women—the group most comparable to our study participants—in Mombasa for 2004 at 10% [22]. The relatively high HIV prevalence in this population may partly explain the high prevalence of HPV infection, HPV58 in particular, and the high proportion of multiple-type infections [23], although it is also known that the Linear Array and Clinical Array HPV tests used in this study are highly sensitive in detecting multiple-type infections [24].

Although not statistically significant, the only independent associations with HPV positivity were found for lifetime number of sexual partners (OR for >3 vs. 1 = 1.5), as was shown in the IARC HPV prevalence surveys [25], and being in a polygamous marriage (OR = 1.7). It is the first time, to our knowledge, that this has been reported.

The high burden of cervical cancer in this region calls for urgent prevention measures. Because cervical cancer screening initiatives with cytology and also visual inspection have been very challenging so far, and also given the high prevalence of HPV infection in the population, we estimate that HPV vaccination might be an innovative and effective way to impact on cancer risk in this African population. In addition, primary screening with HR-HPV testing is being recommended in women over 30–35 years in high-resource countries [26]. HPV testing could also be an effective way of screening in African populations. However, in our study population, around one third of screened women older than 35 years would need triage of HPV-positive test results with a second screening test (e.g., cytology or VIA) and/or colposcopy.

Among the strengths of this study is the age-stratified sampling at the primary health care level across the Mombasa District. This allowed the description of age-specific HPV prevalence in the population. A weakness is the fact that most women were selected opportunistically. Also, a small number of samples (15%) were genotyped by a different test (Clinical Array) than the majority of samples (Linear Array). Both tests, however, seemed comparable with no significant difference in type-specific sensitivity, except for HPV11, which was detected more often with Clinical Array [24].

In conclusion, the findings from this study differ from other world regions, showing a high HPV burden in all age-groups with a high proportion of multiple-type infections. High levels of high-risk HPV prevalence at any age are an important risk factor for cervical cancer incidence. Therefore, our data strengthen the urgency of the introduction of HPV vaccination in Kenya but also highlight the elevated number of women who would have positive results in an HPV-based screening program in the country.

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