Biomolecular and epidemiological aspects of human papillomavirus induced cervical carcinogenesis

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Chapter 2

Ethnic Patterns of Cytological Abnormalities in Cervical Smears in Suriname, a High-Risk Area for Cervical Cancer

Abstract

We determined the prevalence of cytological abnormalities in cervical smears of women attending the first organised screening programme in Suriname and to compare the prevalences in four Surinamese ethnicities with different cervical carcinoma incidence. Cervical scrapes were taken from women with four different ethnicities, i.e. Maroons, Amerindians, Javanese and Hindustani. Papanicolaou staining and cytological screening were performed on 807 cervical smears. Cervical cytological abnormalities were seen in 13.4%, of which 8.1% (62/764) with atypical changes, 2.6% (20/764) with mild and 2.6% (20/764) with moderate and severe dysplasia/CIS. The cytological abnormalities varied between the ethnicities, 42.1% (83/197) in the Maroons and 2.3% (4/176), 5.0% (9/183), and 3.0% (6/208) in the Javanese, Amerindians, and Hindustani, respectively. The high prevalence of moderate and severe dysplasia/CIS in all ethnicities correlates with the high cervical carcinoma incidence in Suriname. A significantly higher prevalence of mild abnormalities in the Maroons was observed, which did not reflect the relatively low cervical cancer incidence in this ethnicity. However, this can be explained by the possibility that these women have a different sexual lifestyle, leading to a higher prevalence of transient HPV infection.

Introduction

Cervical carcinoma is the second most common female cancer throughout the world with considerable differences in incidence rates. Worldwide, over 470,000 new cases are diagnosed yearly and it remains one of the leading causes of death from cancer among women[1-3]. The highest incidence rates are found in developing countries with age adjusted incidence rates of more than 20 per 100,000 women in South America[1-5].

The past decades both the cervical carcinoma incidence as well as the occurrence of the advanced FIGO stages[6] have decreased in developed countries. Screening programme in developed countries account for the majority of this decline in cervical carcinoma incidence and mortality rates although the impact has never been studied in randomised trials[5,7,8]. Decades after the implementation of screening programme, the cervical cancer incidence in the developed countries has decreased 30-60% to age standardised rates between 5.0 and 12.1[1,3-5,8]. Results of a recent case-control study indicated that the substantial decrease in cervical carcinoma incidence and mortality rates in Finland is mainly due to the organised mass screening[9].

Unfortunately, developing countries remain high-risk areas for cervical cancer. They account for 79% of the cervical cancer incidence worldwide and advanced FIGO stages are still of frequent occurrence in these countries[8]. Implementation of screening programmes in developing countries therefore seems an appropriate measure to decrease the high incidence.

Suriname is a high risk area for cervical carcinoma with an incidence of at least 26.7 per 100,000 women and a three- to six fold higher percentage of the advanced FIGO stages (IIB-IV)[10]. There are various ethnicities living in Suriname, which have a different cervical carcinoma incidence. We analysed cervical smears of four different Surinamese ethnicities to determine the prevalence of cytological abnormalities in cervical smears of Surinamese women attending the (preliminary) screening programme that started in 1997. In addition, we investigated whether the differences in cervical cancer incidence existing between the ethnicities was reflected in the proportions of cytological abnormalities.

Material and Methods

Study Population

The smears in this study were collected from Surinamese women attending the (preliminary) screening programme that was part of the bilateral medical care programme between Suriname and the Netherlands. Cervical smears from women of four different ethnicities, i.e. Maroons, Javanese, Amerindians, and Hindustani, were analysed for this study. In former studies about Suriname[10,11] Maroons were called “bush Negroes”. Recently

this ethnicity was renamed. The current name is used in this study. The smears were taken between April 1997 and December 2000 throughout the whole country. Two of our studied ethnicities (Javanese and Hindustani) reside predominantly in urban areas, i.e. Paramaribo, and two (Maroons and Amerindians) reside in the inlands of Suriname. The Maroons and the Hindustani have the lowest cervical carcinoma incidence, the Javanese and the Amerindians have the highest incidence in Suriname[10].

Cervical Smearing

A highly experienced and trained physician (A.G.) supervised and coordinated the practical part of the cervical screening programme. Under his guidance well-trained physicians (assistants) took cervical smears of all the Surinamese women. The majority of the smears were taken in one of the mobile medical units or at a medical clinic in Paramaribo.

A smear sample was taken and spread on two glass slides, fixed and stored at room temperature until use. For every woman a new, disposable cervix brush was used. One glass slide was included in the Surinamese screening programme, the other was shipped to Leiden for review.

Cytological Diagnosis

After shipping the material to Leiden, the Netherlands, standard Papanicolaou staining was performed on all samples for diagnostic purposes. The smears were reviewed by qualified cytotechnologists and a cytopathologist for adequacy, presence of inflammation, pathogens and cytological atypia. Cervical cytological abnormalities were graded using the KOPAC system, the official Dutch microscopical coding system[12,13]. A Pap score was given for communication with clinician and patient. Furthermore, special attention was paid to signs of viral infection, as well as other cervical infections. The term "(cervical) cytological abnormalities" was merely used for atypical or dysplastic changes and not for changes caused by cervical infections.

Statistical Analysis

Odds ratios (OR) and age adjusted ORs with a 95% confidence interval (CI) of cytological findings were calculated for the different ethnicities by using logistic regression. The Hindustani was used as reference ethnicity, because their cervical carcinoma incidence is the average of all ethnicities in Suriname. Both the odds for squamous atypia and higher, and for mild dysplasia and higher were estimated. The reason for this is that smears with squamous atypia can neither be classified normal nor dysplastic. Recent studies show the broad variation of follow-up cytological and histological diagnoses after a first diagnosis of squamous atypia or ASCUS, underlining the necessity of this transition group[14-17].

Results

The age distribution of the four studied ethnic groups is shown in **FIGURE 1**. The median age of the ethnicities was 34 for the Hindustani (mean 35.1 years), the Amerindians (mean 35.8 years), the Maroons (mean 38.1 years) and 34.5 for the Javanese (mean 36.4 years).

Cytopathological Diagnosis

TABLE 1 shows a comparison of four cytological classifications for cervical squamous cells that are frequently used in cytopathology. In the total group 5.3% (43/807) of the smears were unsuitable for cytological evaluation. Cervical cytological abnormalities were detected in 13.4% (102/764) of the assessable smears. Squamous atypia was seen in 8.1% (62/764), mild dysplasia in 2.6% (20/764) and moderate and severe dysplasia/CIS in 2.6% (20/764) of the smears. **TABLE 2** shows the high prevalence of squamous atypia in the

TABLE 1
Comparison of four cytological classifications for cervical squamous cells[27]

Classification	Stage					
Bethesda 2001	NILM	ASC-US ASC-H	(L)SIL	(H)SIL		Invasive carcinoma
CIN Nomenclature	Negative	Squamous Atypia	CIN I	CIN II	CIN III	Invasive carcinoma
Dysplasia Nomenclature	Negative	Squamous Atypia	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia/ CIS	Invasive carcinoma
Papanicolaou Classification	Pap I	Pap II	Pap IIIA*		Pap IIIB/IV	Pap V

*Pap IIIA consists of both mild and moderate dysplasia

TABLE 2
Prevalence of the Cytological Diagnoses in the Assessable Smears per Ethnicity

Ethnicity	No. Tested	Normal Cytology (%)	Squamous Atypia (%)	Mild Dysplasia (%)	Moderate Dysplasia (%)	Severe Dysplasia/ CIS (%)
Maroons	197	114 (58)	57 (29)	15 (7.6)	3 (1.5)	8 (4)
Javanese	176	172 (97.7)	1 (0.6)	3 (1.7)	0 (0)	0 (0)
Amerindians	183	174 (95)	2 (1)	0 (0)	2 (1)	5 (3)
Hindustani	208	202 (97)	2 (1)	2 (1)	2 (1)	0 (0)
All samples	764	662 (86.6)	62 (8.1)	20 (2.6)	7 (0.9)	13 (1.7)

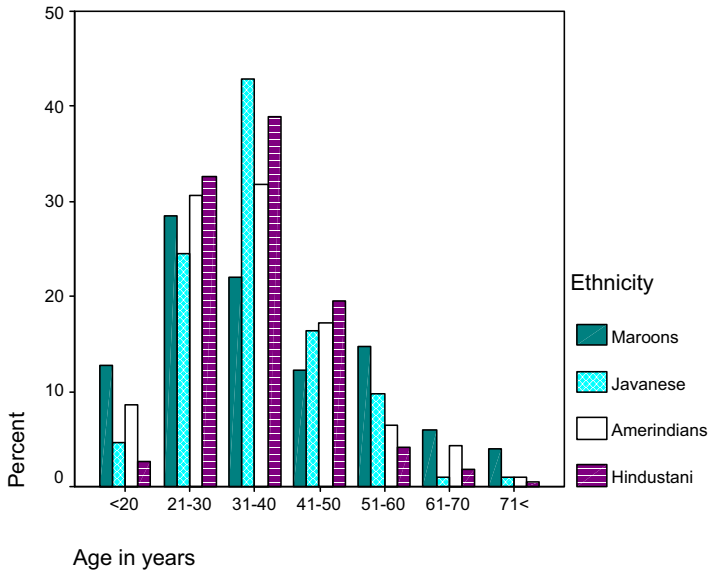

FIGURE 1
Prevalence of the Age Groups per Ethnicity

Maroons (29%) and the lower prevalence in the other ethnicities (1%). It also shows the significantly higher prevalence of mild dysplasia in the Maroons (7.6%) compared to the Hindustani, the Javanese and the Amerindians (1%, 1.7% and 0%). Moderate and severe dysplasia/CIS was observed in respectively 5.5%, 1%, 0% and 4% of the Maroons, the Hindustani, the Javanese and the Amerindians (**TABLE 2**).

The odds ratios and the age adjusted odds ratios of the cytological findings per ethnicity are shown in **TABLE 3**. The odds ratios for squamous atypia and higher is shown in **TABLE 3A**. The highest age adjusted odds ratio of 26.0 (CI 10.7-62.8) was seen in the Maroons. The odds ratios for mild dysplasia and higher are shown in **TABLE 3B**. In the Maroons an age adjusted odds ratio of 8.8 (CI 2.9-26.4) was seen and in the Amerindians an age adjusted odds ratio of 2.13 (CI 0.6-7.4).

Cervical Infections

Virally induced changes, like koilocytosis, were seen in 7.6% of the assessable smears. These changes were present in 2.9% of the Hindustani, 1.7% of the Javanese, 2.2% of the Amerindians and 22.8% of the Maroons (data not shown). In 7.5% of the smears evidence of a Trichomonas infection was seen. In the Hindustani, the Javanese and the Amerindians in 1.4%, 0.6%, and 2.2%, respectively, in de Maroons in 24.9% of the assessable smears. In the Maroons 22.8% of the smears with squamous atypia were infected with Trichomonas (**TABLE 4**).

TABLE 3
Odds Ratios for Cytological Abnormalities in Assessable Smears per Ethnicity

3A. Odds Ratios for Squamous Atypia and Higher

Ethnicity	No. Tested	Sq. Atypia < (%)	OR	95% CI	OR_{adj} [a]	95% CI_{adj} [a]
Maroons	197	83 (42)	24.51	10.37-57.90	25.97	10.74-62.81
Javanese	176	4 (2.3)	0.78	0.23-2.82	0.74	0.21-2.67
Amerindians	183	9 (5)	1.74	0.61-4.99	1.77	0.62-5.10
Hindustani	208	6 (3)	1.00	reference	1.00	reference
[a]Adjusted for age groups						

3B. Odds Ratios for Mild Dysplasia and Higher

Ethnicity	No. Tested	Mild Dyspl. < (%)	OR	95% CI	OR_{adj} [a]	95% CI_{adj} [a]
Maroons	197	26 (13.1)	7.75	2.65-22.66	8.80	2.94-26.38
Javanese	176	3 (1.7)	0.88	0.20-4.01	0.85	0.19-3.86
Amerindians	183	7 (4)	2.03	0.58-7.04	2.13	0.61-7.44
Hindustani	208	4 (2)	1.00	reference	1.00	reference
[a]Adjusted for age groups						

TABLE 4
Prevalence of Trichomonas Infection in the Assessable Smears per Ethnicity and Cytological Diagnosis

Ethnicity	No. Tested	Normal Cytology (%)	Squamous Atypia (%)	Mild Dysplasia (%)	Moder./severe Dysplasia/CIS (%)
Maroons	197	34/114 (29.8)	13/57 (22.8)	2/15 (13.3)	0 (0)
Javanese	176	1/172 (0.6)	0 (0)	0 (0)	0 (0)
Amerindians	183	4/174 (2.3)	0 (0)	0 (0)	0 (0)
Hindustani	208	3/202 (1.5)	0 (0)	0 (0)	0 (0)
All samples	764	42/662 (6.3)	13/62 (21.0)	2/20 (10.0)	0 (0)

Discussion

A high prevalence of moderate and severe dysplasia/CIS was found in this study of a high-risk population for cervical carcinoma. Cervical cytological abnormalities were detected in 13.4% of the assessable smears, of which 2.6% was moderate and severe dysplasia/CIS. In the smears of the Maroons significantly more cytological abnormalities

were detected. Remarkably, their cervical cancer incidence is among the lowest of the Surinamese ethnicities.

In the developed countries the cervical cancer incidence has decreased substantially decades after the implementation of screening programmes[1-5]. The programme in Finland is the model for organised programmes of screening by cervical cytology worldwide[18]. Between the implementation in 1963 and 1990 when the data was established, there has been an 80% decrease in age-adjusted incidence of, and mortality from, cervical cancer[19]. The detection rate of dysplasia in cervical smears in Finland was 0.7% in 1999[20]. In the Netherlands, which is also a low-risk country with a well organised screening programme since decades, moderate and severe dysplasia/CIS was detected in 0.6% in 2001[21].

Since cervical carcinoma is the most common cancer among women in developing countries, the World Health Organization (WHO) recommends the implementation of organised screening programme for cervical cancer in all high-risk areas[5]. In Suriname a nation wide screening programme was initiated in 1998. A high prevalence of cytologically abnormal smears was expected and our study does indeed show a high prevalence of especially moderate and severe dysplasia/CIS. This correlates with the high cervical cancer incidence in Suriname[10].

In Cameroon liquid-based and conventional cytology was compared. ASCUS/LSIL was detected in 10.1%, HSIL in 2.5% (liquid-based cytology)[22]. These prevalences are similar to the prevalences detected in our study. They are higher than the prevalences in the Netherlands[20,21,23]. They are also higher than the prevalences in Finland, another low-risk country, but the ASCUS prevalence is similar to that in Finland[24]. Women with dysplasia will be treated if histological analysis shows CIN and this prevents further carcinogenesis and therefore invasive carcinoma.

In the Maroons a much higher prevalence of squamous atypia and mild dysplasia was present, which could be caused by a possible higher HPV prevalence in this ethnicity. Indeed, HPV-suggesting abnormalities (mainly koilocytosis) were significantly higher among the Maroons (22.6%). This is a strikingly high number when compared with for instance similar data reported from the mass screening in Finland (around 1%)[25,26]. Koilocytosis is associated with clinically active viral infections, the vast majority of which are caused by low-risk HPV types. Koilocytosis becomes progressively more rare among infections caused by high-risk HPV types, which induce a transforming infection with progressive cytological atypia. The productive HPV infections are normally rapidly regressing. Our findings are most feasibly explained by the likelihood of a more active sexual lifestyle among the Maroons. This is manifested as the higher Trichomonas infection rate and the extremely high koilocytosis incidence. The latter relates to a high prevalence of low-risk HPV infections, which results in a high prevalence of predominantly mild abnormalities. As these represent transitory events, they do not necessarily relate to the cervical cancer incidence. The prevalence of moderate and severe dysplasia of the Maroons approached

that of the other ethnicities, which is more in accordance with their relatively low cervical carcinoma incidence. Remaining inconsistencies could be influenced by the fact that our interpretation of abnormalities is limited to cytology alone.

The prevalence rates we found could be influenced by an incomplete attendance and coverage of the population screening in Suriname. The coverage in Suriname for the females in the target age was approximately 50%. Successful screening programmes in developed countries cover at least 60% of the female population at risk, which is screened at regular intervals[8,20,21,23]. There was no significant difference in coverage between the various ethnicities in Suriname.

In conclusion, the high prevalence of moderate and severe dysplasia/CIS in all ethnicities correlates with the high cervical carcinoma incidence in Suriname. The higher prevalence of mild cervical cytological abnormalities in Maroons does not reflect their relatively low cervical cancer incidence. This is, however, likely to be due to a higher transient HPV infection prevalence, most feasibly explained by the likelihood of a more active sexual lifestyle.

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