Age and Ethnic Differences in the Occurrence of Cervical Dysplasia, Cervical Cancer, and Cervical Cancer Deaths in Suriname

Abstract
Background: Updated information on the frequency of premalignant cervical lesions in Suriname is scant, while currently available data on the age and ethnic distribution of cervical dysplasia, cervical carcinoma, and cervical cancer deaths are inconsistent and conflicting. For these reasons, we assessed these topics using a retrospective cohort approach.

Methods and Findings: Using secondary data, the incidence of cervical dysplasia (1995 - 2006) and cervical cancer (1980 - 2008), as well as cervical cancer mortality (1995 - 2010) was estimated and stratified per 10-year age groups and ethnic background. Data were evaluated for statistically significant differences using the Chi-square test and ANOVA, and expressed per 100,000 females per year. There were 2,554 records of dysplasia, 1,117 for cervical carcinoma, and 283 for cervical cancer deaths during the indicated periods. The distribution of cervical dysplasia followed international patterns with a frequency of 1.7% for all lesions and for CIN1, CIN2 and CIN3/CIS of 0.9, 0.5 and 0.3%, respectively. The average cervical cancer incidence was 24 per 100,000 women per year, and the average mortality rate was 10 per 100,000 women per year. The high-risk age groups for overall cervical dysplasia, cervical cancer, and mortality due to this disease were 30-49 (64-71%), 30-59 (60%), and 60-79 years (40%), respectively. Excess risk for cervical cancer and cervical cancer death was seen in Indigenous and Creole women. When compared to the other ethnic groups, Maroon women had the lowest cervical cancer incidence and mortality rates.

Conclusions: Despite incomplete cancer registries, our data suggest that Suriname represents a high-risk country for cervical cancer; that current screening practices have a very limited impact on incidence and mortality; and that high-risk groups are women aged 30-49 years and those of Indigenous and Creole background. These findings support the implementation of more targeted screening programs.

Keywords: Suriname; cervical dysplasia; cervical cancer; cervical cancer deaths; age distribution; ethnic distribution

Introduction
Cancer of the cervix uteri was once one of the most common malignant neoplasms in large parts of the world. However, since the introduction in 1947 of the cytological examination for its early detection - the Papanicolaou or Pap smear [1,2] - the incidence of this malignancy has dramatically declined in particularly industrialized countries [2]. This has resulted in relatively low incidence rates of 6 or less per 100,000 population in Western Asia, Northern America, Western Europe, as well as Australia and New Zealand [3]. As well, the implementation of well-organized and comprehensive cytology-based screening programs in the USA [3] has led to a reduction of the cervical cancer mortality rate from more than 30 to less than 10 per 100,000 population [4].

Unfortunately, cervical cancer is still a major cause of morbidity and mortality in many developing countries [5-7], annual incidence rates amounting up to 70 per 1,000,000 in women over 45 years of age [5]. In these parts of the world, 85% of cervical cancer cases...
and 80% of cervical cancer fatalities are encountered, and this cancer type is responsible for at least 13% of all malignancies in women [3,6]. The differences between industrialized and developing countries probably reflect stark inequalities in health care systems including effective screening programs [5,6,8], and explain to an important extent why cervical cancer is worldwide still the third most common cancer in women and the seventh most common cancer overall [3,9] affecting yearly roughly 530,000 women and killing about 275,000 patients [3].

It is now well-established that high-risk strains of the human papilloma virus (HPV) - particularly subtypes 16 and 18 - are the major causative agents of cervical cancer [5,10-12]. These viruses are sexually transmitted and affect both men and women [5], producing premalignant lesions (‘cervical intra-epithelial neoplasia’ or CIN), the subsequent progression of part of which to overt malignancy occurs through the formation of CIN1 (mild dysplasia), CIN2 (moderate dysplasia), CIN3 (severe dysplasia), and carcinoma in situ (CIS) [2,5,13,14]. The development from CIN1 to CIN3 and subsequently to invasive cancer can take several decades [5]. This is the principal reason that screening for cervical cancer is meaningful, often revealing early-stage disease that is highly treatable.

Other risk factors implicated in the development of cervical dysplasia and cervical cancer include high parity [15,16], long-term use of oral contraceptives [16,17], more than one sexual partner and sexual initiation at an early age [18], tobacco smoking [16,19], the presence of other sexually transmitted infections [20,21], and immunosuppression [22,23]. So far, the involvement of dietary habits in the development of these conditions is not certain.

The Republic of Suriname (South America) has a population of more than 550,000 [24] comprising Hindustanis (originating from East India), Maroons (descendants from runaway slaves shipped from Africa in the 17th century), Creoles (those from mixed black and white origin), Javanese (originating from the Indonesian island of Java), Indigenous Amerindians (the original inhabitants), Chinese, as well as immigrants from Lebanon, Syria, Brazil, and various European countries [24]. Up till now, a relative handful of isolated studies have been conducted on the epidemiology of cervical cancer in Suriname [25-29]. All studies agreed on the relatively high incidence of cervical cancer of more than 20 per 100,000 women per year [25-29]. Furthermore, cervical cancer mortality seemed more or less constant over the last decade [30].

However, estimated frequencies of overall premalignant lesions varied widely, ranging from 1.3 to roughly 5% [25,31,32]. Furthermore, one study reported the highest number of cervical cancer cases (33.7%) in women aged 41 to 50 years [25], while another found no differences in cervical cancer incidence between women of 50 years and older and those aged 20 to 49 years [27,29]. Maroon and Creole/Mixed women would display the highest numbers (42.1%) of cervical abnormalities [31,32], but overt cervical cancers would most commonly occur in Creole and Hindustani [25], Amerindian [26], and/or Javanese women [26-29] while Maroon women would be least likely to develop this malignancy [25-29].

Thus, currently available data on the frequency of premalignant cervical lesions in Suriname are scant, while those on the age and ethnic distribution of cervical dysplasia, cervical carcinoma, and cervical cancer deaths are inconsistent and conflicting. For this reason, we decided to assess these topics in the current study, at the same time determining the age and ethnic groups most at risk to develop cervical dysplasia and overt cancer and to die from this disease. The data obtained are discussed within the framework of international data and possible improvements of screening programs in the country.

**Patients and Methods**

**Study design and study population**

This was a retrospective, descriptive, and exploratory study on the occurrence and the age and ethnic distribution of cervical dysplasia, cervical carcinoma, and cervical carcinoma deaths in Suriname.

**Sources of data**

Data on the occurrence of cervical dysplasia were from Pap test forms from the Lobi Foundation and spanned the period between the years 1995 and 2006. The Pap smears had been evaluated by a trained cytologist and confirmed by a qualified pathologist, and were categorized according to the CIN classification. The Lobi Foundation is a non-governmental organization for reproductive health and the primary institution for cervical cancer screening in Suriname [33]. Together with several public and private primary health care associations and a number of physicians, the foundation covers at least 75% of cervical screening in the country [33]. The Pap test forms contained, among others, information about the date and outcome of the smear, as well as date of birth and ethnic background of the women evaluated. When a woman had undergone repeated tests during one year (re-testing), only the ‘worst’ outcome was recorded. Women who underwent separate tests in different years were separately included in the analysis for each specific year.

Data on the occurrence of cervical cancer were retrieved from the records of the Pathologic Anatomy Laboratory from the Academic Hospital Paramaribo, the only pathology center in Suriname, and covered the period between 1980 and 2008. The Pathologic Anatomy Laboratory is responsible for the evaluation of cytology smears and the histopathological confirmation of patient specimens from all hospitals in Suriname. Cancer cases have been classified using the International Classification of Diseases for Oncology, second edition [34], were digitally available, and included, among others, the histopathological diagnosis, as well as date of birth and ethnic background of the patients. Reporting is estimated to be 80% complete [35].

Information about mortality from cervical cancer was retrieved from the mortality database based on death certificates from the Department of Epidemiology and Biostatistics from the Bureau of Public Health (BOG) of the Ministry of Health. These data were also digitally available, covered the years 1995 through 2010, and included, among others, the cause of death, as well as date of birth and ethnic background of the patients.

Population estimates were derived from data generated by the General Bureau of Statistics [24]. Data on the size of the female population of Suriname stratified according to age were available...
for 1980 (5th census) and 2004 (7th census). Data on the size of the different ethnic groups were only available for the census year 2004. For intercensal years, only non-stratified total mid-year populations were available.

**Data analysis**

The total number of cervical dysplasia between 1995 and 2006, as well as numbers of CIN1, CIN2, and CIN3/CIS cases in this period; the total number of new cervical cancer cases between 1980 and 2008; and the total number of cervical cancer deaths between 1995 and 2010 were recorded. From these data, yearly average numbers of overall cervical dysplasia and CIN1, CIN2, and CIN3/CIS cases; cervical cancer cases; as well as cervical cancer deaths for the indicated periods were calculated.

The proportion of CIN1, CIN2, and CIN3/CIS cases in the population screened between 1995 and 2006 was calculated by dividing the number of CIN1, CIN2, or CIN3/CIS cases by the overall number of smears taken in that period. The proportion of CIN1, CIN2, or CIN3/CIS cases of the total number of positive smears was also calculated.

The average incidence rate for cervical cancer for the period 1980 through 2008 was estimated by dividing the number of newly diagnosed cases by the estimated mid-year female population, and was expressed per 100,000 women. The average mortality rate due to cervical cancer for the period 1995 through 2010 was estimated by dividing the number of deaths by the estimated mid-year female population, and was expressed per 100,000 women.

The age distribution of overall cervical dysplasia and CIN1, CIN2, and CIN3/CIS, cervical cancer and cervical cancer death has been presented as the number of cases per 10-year age group with respect to the total number of cases in the indicated periods.

Data on the ethnic distribution are presented for the four main ethnic groups in Suriname, viz. Hindustani, Creoles, Javanese, and Maroons, comprising about 27, 18, 16, and 14%, respectively of the population of Suriname [24]. Although comprising only 3.7% of Suriname’s population [24], data for the Indigenous women are also presented, because previous studies [26] suggested that these women may run a relatively high risk to develop cervical cancer and die from this condition. The ethnic distribution of overall cervical dysplasia and CIN1, CIN2, and CIN3/CIS, cervical cancer, and cervical cancer death has been presented as the number of cases per ethnic group with respect to the total number of cases in the indicated periods. In addition, for each ethnic group, incidence and mortality rates of cervical cancer were calculated, by dividing the number of cases between 1980 and 2008, or the number of deaths between 1995 and 2010, respectively, by the estimated female population size (all ages) of that ethnic group in the indicated period, and expressed per 100,000 women per year.

**Statistics**

Data are presented as absolute numbers and as means ± SDs. The mean ages among groups of women with different degrees of cervical dysplasia were compared using the one-way ANOVA test. Incidence and mortality rates for cervical cancer among the different ethnic groups were compared using the Chi-square test. P values < 0.05 were taken to indicate statistically significant differences.

**Ethical considerations**

The study was approved by the Ministry of Health. The collected data were entered into a password-protected electronic database and kept confidential. The risk of violation of confidentiality was minimized by storing the database in a separate location. It was furthermore agreed to hand the database over to the Lobi Foundation after analysis.

**Results**

**Generalities**

A total of 144,846 women were screened for cervical dysplasia between the years 1995 and 2006. This led to the identification of 2,518 cases of cervical dysplasia (Table 1), indicating that about 1.7% of the screened population was positive. The number of positive cases decreased with increasing degree of dysplasia: CIN1 was seen in more than half of cases, CIN2 in almost one-third of cases, and CIN3/CIS in less than one-fifth of cases. Thus, these lesions occurred in approximately 0.9, 0.5 and 0.2% respectively of the screened population.

There were 1,494 new cases of cervical cancer between 1980 and 2008 (Table 1). This corresponded with approximately 52 new cases per year or 1 new case per week (Table 1), and an average incidence rate for this period of 24 ± 5 per 100,000 females per year.

Three hundred and fifty-eight women died from cervical cancer between 1995 and 2010 (Table 1). Thus, in this period, there were roughly 20 cervical cancer deaths per year (Table 1), or almost 2 per month. This led to a mortality rate for the period covered by this study of 10 ± 3 per 100,000 women per year.

**Age distribution of cervical dysplasia, cervical cancer, and deaths due to cervical cancer**

The mean age of the women who had tested positive for a dysplasia was approximately 39 years (Table 1). That of women with a CIN1 or a CIN2 was in the same order of magnitude (Table 1), while that of women with a CIN3/CIS was on average 43 years (Table 1). Apparently, women older than 40 years were more likely to suffer from more advanced cervical lesions when compared to those younger than 40 years.

As shown in Table 2, both the number of overall dysplasia and the different degrees of dysplasia increased with increasing age, peaked in the age group between 30 and 39 years, and then declined gradually to almost zero in women of 80 years and older. Notably, around 65% CIN categories as well as overall dysplasia was in women aged between 30 and 49 years (Table 2), indicating that more than two-thirds of cervical dysplasia occurred in women younger than 50 years of age.

The mean age of women diagnosed with cervical cancer between the years 1980 and 2000 was 52 ± 15 years (Table 1). There were relatively few cases before age 30 years, but the frequency increased sharply in the age group 30-39 years, peaked in the age group 40-49 years, then decreased gradually in the subsequent age groups (Table 2). Notably, about one-third of women...
suffering from cervical cancer was 50 to 69 years old (Table 2), but almost half was younger than 50 years of age (Table 2). These observations suggest that women younger than 50 years of age ran the same risk to contract cervical cancer as women older than 50 years. The mean age of cervical cancer deaths in the period between 2000 and 2010 was 58 ± 15 years (Table 1). Almost two-thirds of fatalities were 50 years and older (Table 2). However, more than one-third was younger than 50 years of age (Table 2) with a peak (one-quarter of the total number) aged between 40 and 49 years (Table 2). Thus, although most cervical cancer deaths were older women, a substantial number of fatalities occurred at a younger age.

Ethnic distribution of cervical dysplasia, cervical cancer, and deaths due to cervical cancer

Table 3 shows that in all ethnic groups the number of cervical dysplasia decreased with increasing degree of abnormality. There were, furthermore, no or only slight differences among the ethnic groups with respect to the occurrence of either type of lesion. On the other hand, most cases of cervical cancer were in Creole, Hindustani, and Javanese women (35, 30, and 22% respectively of the total number; Table 3). However, when expressed with respect to the estimated female population size of each ethnic group, cervical cancer incidence turned out highest in Creole and Indigenous women, namely about 38 per 100,000 per year (Table 3). These values were almost 60% higher than the above-
Table 3 Ethnic distribution of cervical dysplasia (1995 to 2006), cervical cancer (1980-2000), and deaths due to cervical cancer (2000 to 2010) in Suriname. Percentages of total numbers are given between brackets.

| Ethnic group | Dysplasia | Cervical cancer cases | Cervical cancer deaths |
|--------------|-----------|-----------------------|-----------------------|
|              | CIN 1 (% of total number) | CIN 2 (% of total number) | CIN 3/CIS (% of total number) | Overall dysplasia (% of total number) | Number of cancer cases (% of total number) | Ethnic-specific incidence rate | Number of deaths (% of total number) | Ethnic-specific mortality rate |
| Hindustanis  | 351 (58)  | 151 (25)  | 108 (18)  | 610 (100)  | 294 (30)  | 21  | 68 (26)  | 9  |
| Creoles      | 360 (57)  | 171 (27)  | 104 (17)  | 635 (100)  | 343 (35)  | 38  | 69 (27)  | 15 |
| Javanese     | 162 (50)  | 97 (30)   | 63 (20)   | 325 (100)  | 214 (22)  | 29  | 64 (25)  | 17 |
| Maroons      | 161 (49)  | 34 (31)   | 65 (20)   | 260 (100)  | 66 (7)    | 8   | 35 (13)  | 8  |
| Indigenous   | 49 (44)   | 34 (31)   | 28 (25)   | 111 (100)  | 71 (7)    | 38  | 24 (9)   | 24 |
| Total        | 1,083 (100) | 487 (100) | 368 (100) | 1,941 (100) | 988 (100) | -   | 260 (100) | -  |

1Expressed with respect to the total female estimated population size all ages for the period 1980 to 2000 of each ethnic group (Hindustanis: 1,387,764; Creoles: 907,410; Javanese: 736,008; Maroons: 812,280; Indigenous: 188,748); data are per 100,000 women of each ethnic group per year

2Expressed with respect to the total estimated female population size all ages for the period 2000 to 2010 of each ethnic group (Hindustanis: 726,924; Creoles: 475,310; Javanese: 385,528; Maroons: 425,480; Indigenous: 98,868); data are per 100,000 women of each ethnic group per year

3Not significantly different from the average overall cervical cancer incidence rate of 24 (p values of 0.0542, Chi²)

4Significantly higher than the average overall cervical cancer incidence rate of 24 (p values < 0.0001, 0.0002, 0.0079, Chi²)

5Significantly lower than the average overall cervical cancer incidence rate of 24 (p value < 0.0001, Chi²)

6Not significantly different from the average overall cervical cancer mortality rate of 10 (p values of 0.42 and 0.18, Chi²)

7Significantly higher than the average overall cervical cancer mortality rate of 10 (p values 0.013, 0.0007, and < 0.0001, Chi²)

mentioned overall average rate for this period of about 24 per 100,000 females per year. The lowest incidence rate (8 per 100,000 women per year) was in Maroon women (Table 3). This value was three times lower than the overall average of 24, and almost five times lower than that found for Creole and Indigenous women. Cervical cancer incidence rates in Hindustani and Javanese women were in the range of the overall average of 24, but still clearly higher than that found for Maroon women (Table 3). Apparently, the risk to develop cervical cancer was highest in Creole and Indigenous women, but lowest in Maroon women.

Information about the ethnic background of the patients who had died from cervical cancer in the period covered by this study was available for 260 women (Table 3). As found for the occurrence of cervical cancer (Table 3), most fatalities due to this disease were Creole, Hindustani, and Javanese women (27, 25, and 25%, respectively of the total number; Table 3). But again, when expressed with respect to the estimated female population size of each ethnic group, cervical cancer mortality appeared highest in Indigenous women, viz. 24 per 100,000 women per year (Table 3). This was approximately twice higher than the above-mentioned overall average mortality rate for this period of about 10 per 100,000 women per year. The mortality rate in Creole and Javanese women was also clearly higher than the overall average, while that in Hindustani and Maroon women was close to this value.

**Discussion**

In this study on the epidemiology of cervical cancer in Suriname, overall cervical dysplasia were found to occur at a frequency of 1.7% of the screened population; overt cervical carcinoma at a rate of 24 ± 5 per 100,000 women per year, and cervical cancer mortality at a rate of 10 ± 3 per 100,000 females per year. Moreover, clear differences in the age distribution of cervical dysplasia, as well as in the age and ethnic distribution of cervical cancer incidence and cervical cancer mortality were found. The mean age of women with a CIN1 or CIN2 was approximately 39 years and that of women with CIN3 or CIS 43 years, while cervical cancer occurred at a mean age of 51 years, and death due to this disease at the mean age of 59 years. Furthermore, most CIN3 and CIS were in Indigenous women; cervical cancer was most common in Creole and Indigenous women and least in Maroon women; and most cervical cancer fatalities were in Indigenous, Javanese, and Creole women, and least in Hindustani and Maroon women.

The occurrence of overall cervical dysplasia in 1.7% of the screened population, and the detection of CIN1, CIN2, and CIN3/CIS in 0.9, 0.5, and 0.3%, respectively of evaluated women, is in accordance with international patterns [8,18]. However, the national screening coverage of Suriname between 1990 and 2010 ranged from 1 to 13% with an average of 7 ± 2% [8,18]. This low coverage in the current study suggests that the presented estimates might represent an underestimation of absolute numbers. It can be argued that the distribution may be different with a better screening coverage. More importantly, for a cervical cancer screening program to be effective and to bear a substantial impact on both incidence and mortality, a coverage of at least 80% must be achieved [5,8]. As the coverage in Suriname clearly falls far behind this target number, it is understandable that current screening practices have very limited impact on cervical cancer incidence and mortality in the country. Indeed, the average annual
cervical cancer incidence and mortality rate of about 24 and 10, respectively, have been reported before [26, 27] and classify Suriname as a high-risk country for this malignancy. Markedly, Suriname is among the Latin American and Caribbean countries with the highest cervical cancer incidence rates [6].

The high-risk age groups for overall cervical dysplasia lesions, cervical cancer, and death from cervical cancer were those of 30 to 49 years (64-71% of the total number of cases), 30 to 59 years (60% of the total number of cases), and 60 to 79 years (40% of the total number of cases), respectively. This age distribution is also in accordance with international patterns [8,18]. Furthermore, the mean age of 39 years for the low-grade lesions, and the tendency for high-grade lesions and cervical cancer to occur in older women (at a mean age of 43 and 53 years, respectively), have also been observed in other countries with a cervical cancer incidence comparable to that of Suriname [33]. Notably, the occurrence of almost half of cervical cancers in women younger than 50 years of age and about one-third in women aged between 50 and 69 years, together with the observation that most cervical cancer deaths were in women aged between 40 and 79 years, supports that screening practices do not reach sufficient women to prevent the disease, and that this deficit could be responsible for the many cases and deaths in older women.

We found no ethnic differences in the distribution of cervical dysplasia, although a previous study [31] had reported more low-grade lesions in Maroon women when compared to women of other ethnic backgrounds. This discrepancy cannot be readily explained from our observations. However, in the current study, overt cervical cancer was significantly more common in Indigenous and Creole women than in women from other ethnic backgrounds, and cervical cancer mortality was highest in Indigenous women, followed by Javanese and Creole women. Maroon women were found to run the lowest risk to develop cervical cancer and to die from this disease.

The excessively high cervical cancer incidence and mortality rate in Surinamese Indigenous women observed in this study is in accordance with the results from previous studies [25,26]. Our observations are also in line with those for the Indigenous populations of Guyana [34], Ecuador [35,36], and Australia [37-39]. These populations are consistently exposed to well-established risk factors for cervical cancer such as young age at first intercourse, early onset of childbearing, high parity, promiscuity, increased exposure to HPV infection and other sexually transmitted diseases, cigarette smoking, low socio-economic status, limited access to health services, and late-stage disease [34-39]. At least some of these risk factors also apply to Surinamese Indigenous women [40], providing a possible explanation for their relatively high risk to develop cervical cancer and to die from this malignancy.

The higher incidence of cervical cancer in Creole women when compared to women from other ethnic groups noted in the current study is in agreement with the previously mentioned apparent predilection of this ethnic group for several cancer types including cervical cancer [27,28]. As yet, these observations cannot be satisfactorily accounted for. However, in the USA, cancer was more frequently seen in African-Americans than in other ethnic groups, overall incidence rates for the former group being 10%, 50 to 60%, and more than twice higher than those for Caucasians, Hispanics and Asian/Pacific Islanders, and American Indians, respectively [41-43]. And in the case of cervical cancer in Suriname, the greater exposure of Creole women to risk factors such as high parity, early age at first sex, and early pregnancies when compared to women from other ethnic groups may render them more susceptible to this malignancy [44]. Clearly, this subject should be investigated in greater detail in future studies.

Kril et al. reported a remarkably high incidence rates for cervical cancer among Indigenous and Javanese women [26]. In our study, the highest rates were seen in Creole and Indigenous women, followed by Javanese women. These differences may be attributed to the different time periods studied and the possibility of misclassification of ethnic background. Indeed, information on ethnic background in most Surinamese studies is based on appearance and surname of, and/or self-reporting by subjects [24, 26]. This also held true for the current study for which secondary data have been used and no control could be exercised on the classification of subjects. Therefore, the results on ethnic distribution should be interpreted with some caution.

Still, as reported for Creole women, Maroon women have their first sexual encounter and their first child at a mean age of 16 years [44]. Furthermore, like Indigenous women, Maroon women share multiple partners and undergo less screening for cervical lesions than women from other groups [44], while their unusual vaginal hygiene practices - herbal steam baths to enhance the appearance and health of their vagina [45] - may predispose them more to HPV infection than women from other ethnic groups [44,45]. With this background, the relatively low risk of Maroon women to develop cervical cancer and to die from this disease noted in the current study cannot be readily explained. It is conceivable that these women are protected from developing cervical cancer by so far unknown genetic and/or behavioral factors [31]. It is also possible that their infections are mainly caused by low-risk HPV subtypes which may cause dysplasia but neither in situ nor overt cancer [31]. Obviously, both these suggestions must be further explored.

Summarizing, the results from the current study indicate that screening practices in Suriname had so far limited or no impact on the occurrence of cervical cancer and death due to this disease in the country. Incidence and mortality rates in the country are still among values associated with high-risk regions for cervical cancer, indicating that Suriname has a serious public health problem with this disease. Women aged between 30 and 49 years and those from Indigenous and Creole background run the highest risk to develop cervical cancer and to eventually die from this disease. These observations indicate a need to improve existing screening practices and support the implementation of targeted screening programs.

Acknowledgements

The authors wish to express their gratitude to A. Grünberg, MD, PhD, Medical Director Lobi Foundation; G. Leckie, PhD, General Director Lobi Foundation; and Mrs. Karlien, Head of Cytology, Lobi Foundation, for their permission to and support during the collection of data at their institution.
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