International Journal of Gynecology and Obstetrics 120 (2013) 257–261

Contents lists available at SciVerse ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

CLINICAL ARTICLE

Effect of 2 referral intervals on diagnostic discordance between cytology and histology at a colposcopy clinic

Francois Saayman [a,*], Cyril J. Van Gelderen [a], Pam Michelow [b], Eunice J. Van Den Berg [c], Yasmin Adam [a]

[a] Department of Obstetrics and Gynecology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa
[b] Cytology Unit, Department of Anatomical Pathology, Faculty of Health Sciences, University of the Witwatersrand, National Health Laboratory Services, Johannesburg, South Africa
[c] Department of Anatomical Pathology, Faculty of Health Sciences, University of the Witwatersrand, National Health Laboratory Services, Johannesburg, South Africa

ARTICLE INFO

Article history:
Received 19 June 2012
Received in revised form 21 September 2012
Accepted 16 November 2012

Keywords:
Cervical dysplasia
Colposcopy
HIV
Papanicolaou smear
Referral interval
South Africa

ABSTRACT

Objective: To determine the effect of the time interval between cervical cytology screening and histology at treatment on grade of cervical disease. *Methods:* In a retrospective cross-sectional study at a colposcopy clinic in Soweto, Johannesburg, South Africa, data were compared from women with cytologic abnormalities referred for colposcopy between April 2003 and June 2010 to determine whether early (≤180 days) or late (>180 days) referral had an impact on dysplasia grade. *Results:* In the early and late referral groups, there were 213 (13.43%) and 201 (14.63%) women, respectively, with upgrading of cervical dysplasia ($P=0.35$), and 1373 (86.57%) and 1173 (85.37%) women, respectively, with downgrading or no change ($P=0.35$). Risk factors for upgrading were HIV infection (odds ratio [OR], 1.63; $P<0.001$) and condom use (OR, 1.30; $P=0.02$). Four cases (0.68%) of invasion among women with low-grade squamous intraepithelial lesion (LSIL) and 50 cases (2.11%) among women with high-grade SIL (HSIL) were not detected by cytology. Risk factors for invasive disease on histology were age (OR, 1.09 per year; $P<0.001$), parity (OR, 1.32 per pregnancy; $P<0.001$), and HSIL on cytology (OR, 3.17; $P=0.03$). *Conclusion:* There was no difference in the up- or downgrading of cervical dysplasia between the 2 referral groups.

1. Introduction

Cervical cancer is a major health concern in South Africa and other low-resource countries. The overall crude incidence of cervical cancer in southern Africa in 2010 was 22.5 cases per 100 000 women, as compared with 15.8 cases per 100 000 women globally [1].

Prevention of cancer of the cervix has become a national health priority in South Africa, where screening for cancer precursors with the Papanicolaou (Pap) smear began in 2001 [2]. In South Africa, the screening program recommends that cervical cytology should be performed 3 times in a woman's lifetime at 10-year intervals starting at 30 years of age [2]. This program might prevent approximately two-thirds of cervical cancers [3].

For cervical cancer prevention to succeed, all aspects of the service need to be functional: namely, screening, diagnosis (colposcopy and biopsy), treatment, and follow-up. Colposcopy services are limited and overwhelmed by the large number of referrals, resulting in delayed diagnosis and treatment.

Guidelines in the UK state that women should be examined in a colposcopy clinic within 2 weeks if their tests indicate suspected cancer or glandular neoplasia, 4 weeks if they indicate high-grade disease, and 8 weeks if they indicate low-grade disease [4]. The cervical cancer screening program in South Africa does not stipulate a time frame within which a patient should be seen.

Fakokunde and Selo-Ojeme [5] showed that, among 316 women with high-grade smears, those seen after 180 days were less likely to need excisional treatment (33.8% versus 55.8%; odds ratio [OR], 0.45; 95% confidence intervals [CI], 0.25–0.78; $P<0.001$) and less likely to have high-grade disease (24.3% versus 45.9%; OR, 0.37; 95% CI, 0.21–0.68; $P<0.001$) as compared with women seen before 180 days. No significant difference between the 2 groups of women was found with respect to invasive disease [5].

In addition, Kirby et al. [6] considered that mild (cervical intraepithelial neoplasia grade 1 [CIN1]) or moderate (CIN2) dyskaryotic smears should not be an indication for immediate referral for colposcopy because, under a conservative management policy, most women return to normal without treatment.

The ideal time frame within which a patient with abnormal cervical cytology should attend colposcopy is not known. This situation is complicated by the fact that not all lesions will progress, and in fact some may regress [7,8]. The aim of the present study was therefore to investigate the impact of referral interval on final histology. The

* Corresponding author at: Chris Hani Baragwanath Academic Hospital, Postnet Suite 28, Pvt. Bag X1569, Johannesburg, Glenvista, 2058, South Africa. Tel.: +27 784588686; fax: +27 11 682 1447.
E-mail address: fsaayman@hotmail.com (F. Saayman).

0020-7292/$ – see front matter
http://dx.doi.org/10.1016/j.ijgo.2012.09.022

study also investigated the effect of HIV on dysplasia and attempted to determine other risk factors for upgrading and invasive disease.

2. Materials and methods

In a retrospective cross-sectional analysis, data collected between April 3, 2003, and June 30, 2010, at the colposcopy clinic at Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg, South Africa, were analyzed. Written consent for colposcopy and use of the data for research purposes was obtained from all patients. The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg, South Africa (M10530, May 2010).

The study data collected included information on demographic details, HIV status, date and result of cervical cytology, colposcopy findings, date of treatment, and histology results. Cervical cytology was assessed by conventional Papanicolaou (Pap) smear and reported by the National Health Laboratory Service using the Bethesda classification [9].

Women with high-grade squamous intraepithelial lesion (HSIL) or worse, those with persistent low-grade squamous intraepithelial lesion (LSIL) (2 or more consecutive smears), and HIV-positive women with any abnormality were referred to the colposcopy clinic.

To save time and cost, and to minimize loss to follow-up, the colposcopy clinic practices a policy of "see and treat", by which all women with cervical cytology showing HSIL or worse, coupled with either colposcopy suggesting CIN2 or worse or an inadequate colposcopy result, are treated with immediate large loop excision of the transformation zone (LLETZ). In addition, HIV-infected women with cervical cytology showing LSIL or worse, coupled with colposcopy of CIN1 or worse, are also treated immediately owing to the uncertainty of disease progression for these women.

Ideally, 2 histologic specimens should be compared to determine the progression or regression of disease. When comparing cytology to histology, it is possible only to comment on the diagnostic discordance between the 2 findings. To describe this discordance, the term "upgrading of dysplasia" was used when cervical cytology showed LSIL and histology showed at least CIN2, or when cervical cytology showed HSIL and histology showed invasion. "Downgrading of dysplasia" was defined as HSIL or LSIL on cervical cytology coupled with normal histology, or HSIL on cytology coupled with CIN1 or less on histology.

Data were extracted from the colposcopy database on November 10, 2010, and coded for analysis. Missing data and outliers were rechecked on the National Health Laboratory Service system and on the CHBAH record database for accuracy. Duplicate records were deleted.

The HIV status recorded in the database was not always confirmed. Women who reported having had a negative test within 6 months of their visit were regarded as negative. HIV testing was offered to all patients only from 2006 onward. Owing to stigmatization, many HIV-positive patients might have chosen not to disclose their status. As a result, the incidence of HIV reported in the study might have been underestimated.

The patients were divided into 2 referral groups of 180 days or shorter, and longer than 180 days. It would be unethical to randomize patients into a referral interval of more than 180 days, but it was possible to use this interval in the study owing to the existing long and variable waiting time in the South African public sector. The referral interval was calculated from the date of cervical cytology screening until the day of the first visit to the colposcopy clinic. The change in severity of dysplasia between the 2 groups was compared.

Stata version 10 (StataCorp, College Station, TX, USA) was used to analyze data. Categoric variables were described via frequencies, and continuous variables via means and medians. The t test was used for comparisons of continuous data, and the χ^2 test was used for proportions. A logistic regression was performed to find factors associated with upgrading of dysplasia and invasive disease on histology. A P value of less than 0.05 was considered statistically significant.

3. Results

During the study period, 3942 women were referred to the CHBAH colposcopy clinic. Data were excluded from 982 women for various reasons (Fig. 1); as a result, 2960 women were included in the analysis.

Most of the women were referred to the clinic for HSIL (65%) or LSIL (17%). Invasion was suggested by cytology in 3.40% of the women referred (Fig. 2).

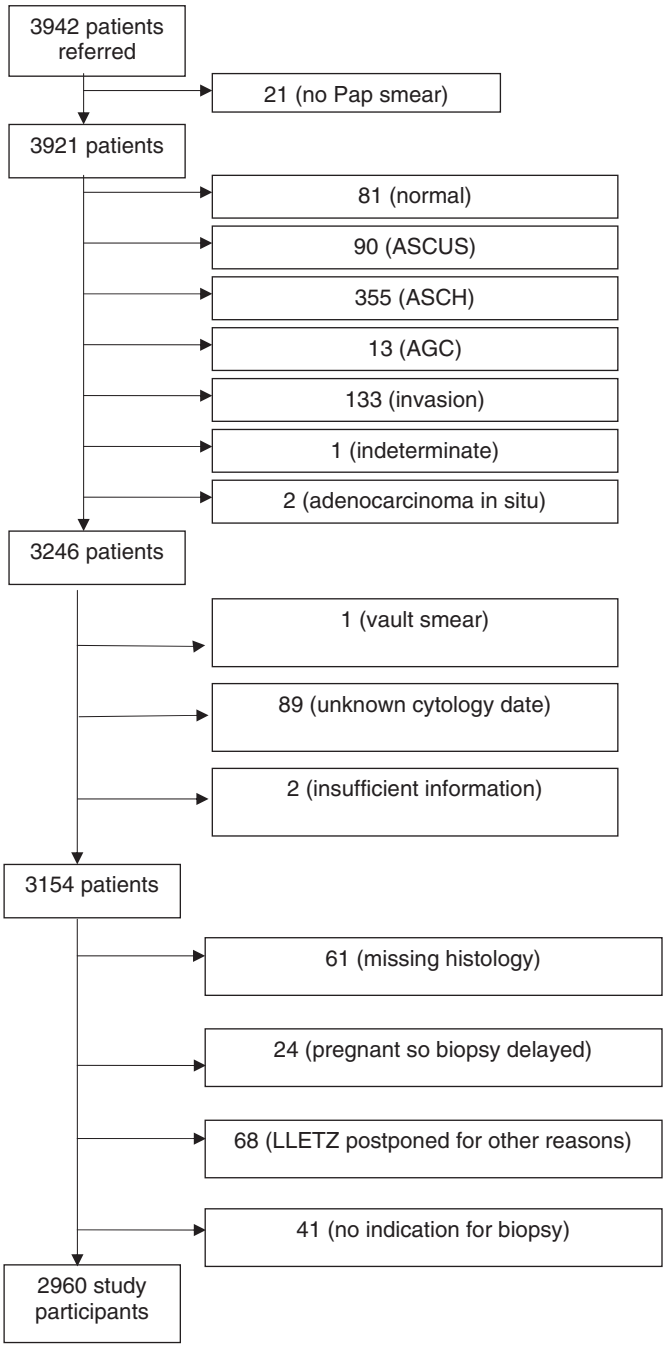

Fig. 1. Summary of patients excluded from the analysis.