ORIGINAL RESEARCH ARTICLE

Audit of Cervical Cancer Screening and Colposcopy Attendance in Rural South Africa

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Abstract

Women in developing countries generally lack access to cervical cancer preventive services. An audit was performed in rural South Africa to test the hypothesis that women do not follow (pre-)cancerous cervical disease treatment sufficiently, to understand the possible reasons for this non-attendance behavior, and to evaluate other published diagnostic and treatment initiatives. Based on Pap smear and colposcopy attendance data, including age, HIV status, month of attendance, and cervical intraepithelial neoplasia (CIN) staging, relatively few patients (54% of 928 patients) visited a colposcopy clinic following an abnormal Pap smear. Although these co-factors do not explain this high non-attendance rate, HIV status was an important co-factor; percentage-wise, HIV positivity correlated with a higher attendance rate. Screening methods that use mobile teams to successfully deliver cost-effective on-the-spot treatment warrant further attention. *(Afr J Reprod Health 2014; 18[4]: 70-78).*

Keywords: cervix, cancer, HIV, preventive screening, colposcopy, South Africa

Résumé

Les femmes des pays en développement n'ont généralement pas accès aux services de prévention du cancer du col utérin. Une vérification a été réalisée en Afrique du Sud rurale pour tester l'hypothèse que les femmes ne suivent pas le (pré) traitement de la maladie cancéreuse du col suffisamment pour comprendre les raisons possibles de ce comportement de la non présence et d'évaluer d'autres initiatives diagnostic et de traitement publiées. Se basant sur les analyses de Papanicolaou et les données de fréquentation de la colposcopie, y compris l'âge, le situation du VIH, le mois de fréquentation, et la néoplasie intra épithéliale cervicale (NIC) de mise en scène, relativement peu de patientes (54% des 928 patientes) ont visité une clinique de colposcopie suite à un frottis anormal. Bien que ces co-facteurs ne expliquent pas ce taux de non-participation élevé, l'etat du VIH était un co-facteur important; en pourcentage, la séropositivité corrélée avec un taux de participation plus élevé. Les méthodes de dépistage qui se servent des équipes mobiles pour livrer avec succès un traitement rentable et sur le terrain méritent une attention particulière. *(Afr J Reprod Health 2014; 18[4]: 70-78).*

Mots-clés: col, cancer, dépistage préventif, colposcopie, Afrique du Sud VIH

Introduction

Annually, approximately 500,000 women worldwide are diagnosed with cervical cancer, and daily more than 700 women die from this disease[1]. The majority of these fatalities occur in the developing world. The prevalence of invasive cervical cancer peaks in the sixth decade of life, and the mortality rate is >50% in all age groups[2]. Approximately one in every 40 women will develop cervical cancer within their lifetime[3]. In South Africa, cervical cancer is the second-most common cancer (after breast cancer) the prevalence in 2008 was 6,500 per 100,000, and the mortality rate was 3,467 per 100,000[4].

Although the cervix is a target for carcinogenic factors such as human papillomavirus (HPV), no form of cancer better documents the remarkable benefits of early diagnosis and curative therapy on mortality rate than cervical cancer[5].

Contrary to women in industrialized countries who have relatively easy access to cervical cancer screening services, women in developing countries generally lack access to such programs. Furthermore, the often insufficient infrastructure and lack of awareness among both the hospital

staff and the target population of the importance of screening and treatment make managing pre-cancerous cervical lesions even more difficult. To combat this disease, preventive and treatment programs should be evaluated. At the same time, attendance behavior for colposcopy (a method for diagnosing and treating cervical abnormalities and lesions that could lead to cervical cancer) should be sufficient to achieve a good prognosis.

Performing a Pap smear to detect cervical abnormalities is the best-known form of secondary prevention[6]. South Africa relies on Pap smears as a primary screening tool[7]. We hypothesized that the majority of women with an abnormal Pap smear despite being informed of this result by their healthcare professional and referred for colposcopy failed to attend for colposcopy and further treatment. We examined the reasons for non-attendance and evaluated the published literature to study the quality and success of screening and treatment methods that use mobile teams to reach women in rural areas.

We tested the following four hypotheses with respect to non-attendance at a colposcopy clinic: 1) HIV infection is correlated with cervical cancer as a comorbidity factor[8]; 2) increasing age is correlated with a higher non-attendance rate; 3) there is a correlation between the severity of abnormal lesions and disease progression (CIN staging); and 4) attendance is decreased in colder months. Literature and prior research materials were also studied in order to evaluate the approach of mobile teams and the use of visual inspection of the cervix using acetic acid (VIA).

Methods

Study design

An audit of the existing system for screening and managing patients with abnormal cervical smears was performed in East London, South Africa, in collaboration with the National Health Laboratory Services (NHLS). The audit was performed using data obtained from patient files from two district hospitals, Frere Hospital and Cecilia Makiwane Hospital (CMH).

The hospital management was informed of the audit and the aim of the study. The protocol was approved by the East London Hospital Complex Ethics Committee, and the electronic information was studied in order to select abnormal Pap smears and the colposcopy biopsy results of women who attended clinics from the drainage area of Frere Hospital and CMH in the Eastern Cape from January 2006 through December 2007.

We focused on data regarding the pre-cancerous stages of cervical cancer (i.e., CIN stage II or III) and cancerous stages (if diagnosed as such). The CIN stages were used as established by the International Federation of Gynecological Oncology. CIN I and II are prone to regression and are curable if diagnosed in time[9]. The new Bethesda classification system, in which the precursors are named squamous intraepithelial lesions (SIL), has now been implemented in the National Screening Guideline in South Africa; however, this classification system was not used when the data were collected. Low grade SIL (CIN I) do not require a first-time referral but a repeat Pap smear in 12 months[10]. Thus, the NHLS CIN I category was not registered; the data included in our study were from patients who had a first-time abnormal Pap smear and first-time colposcopy results and therefore either had CIN II or worse.

Study material

The referral guideline for colposcopy in South Africa is as follows: the South African national cervical screening policy is based on the use of cervical cytology and recommends that all women age 30-60 years receive a Pap smear every ten years[11]. Therefore we used Pap smears as a subject for this study.

Only data from patients with a positive Pap smear (i.e. patients who required a colposcopy) were extracted from the NHLS database. In total, laboratory results for Pap smears and cervical biopsies of 928 patients were collected.

The collected data included the patient's name and hospital record number, the source of the specimen, cytology results, and/or histology results. Other relevant information including HIV infection and treatment status, age, time of year, CIN stage and cancer progression was also used. Colposcopy attendance data were collected using the matching record numbers from patients with an

abnormal Pap smear. It included the type of cervical abnormality, lesion grading, and disease classification.

HIV and cervical cancer are closely correlated; women have a 4.9 fold higher risk of developing cervical cancer than HIV-negative women[12-13-14]. Although the NHLS data regarding HIV was dependent on the completeness of information provided by the referring clinicians, they were included in the present study as a factor to estimate its value as a potential co-morbidity factor that could influence non-attendance.

Statistical analysis

Patient data were analyzed to estimate their significance regarding attendance behavior for colposcopy and to evaluate their role in the patient's decision regarding whether to attend for treatment. Concerning HIV and month-dependent attendance, we excluded the data from the first three months (only two patients available) in order to increase the power of our statistical analysis.

The rationale for analyzing the four co-factors was as follows

HIV status

We analyzed the data regarding HIV status in order to test whether treatment behavior is affected by HIV infection. Data were collected with the prior knowledge that HIV co-infection with HPV can contribute to a higher level of lesion formation (in terms of both CIN staging and cancer severity) within the cervix[15], with an expectation that there would be a high prevalence of HIV within the patient population[16]. Moreover, women with HIV infection are less compliant with respect to seeking treatment due to a possible fear of stigmatization or taboo[17]. Thus, HIV positivity may be a strong contributing factor to non-attendance behavior.

Age

Prior to our audit, we considered the possibility that age can influence treatment compliance. The expectation was that younger women would be more likely to attend for colposcopy and treatment because they are more educated than older women, and thus more aware of the possible consequences of HPV infection and of preventive medicine (such as HPV vaccination) and regular screening for cervical cancer[18].

Prior to this study, we found no published age-related research with respect to attendance behavior. Moreover, studies were inconsistent with respect to the correlation between age and cancer incidence and/or severity. Therefore, age data were included in this audit for impact analysis.

CIN staging and lesion severity

Pre-cancerous cervical lesions are classified into stages that reflect the severity of the lesion's formation. Based on international consensus, lesions can be classified into three categories: lesions with mild dysplasia (LSIL or CIN I), which were not included in the original NHLS data; lesions with moderate dysplasia (HSIL or CIN II); and lesions with severe dysplasia (HSIL or CIN III).

The original NHLS data contained additional coded sub-categories which were redefined for our statistical analyses. Therefore, several categories were created: CIN II (severe dysplasia with or without HPV), CIN III, and CIN III with early carcinoma. Adenocarcinomas and squamous-cell carcinomas were categorized separately, as these two cancer types differ in prognosis, with adenocarcinoma having a lower survival rate[19]. Other forms of cancer were also included in a separate category "Other" (all types of cervical diseases, incompletely named diseases, etc.).

Time of year (i.e., month of attendance)

With no *a priori* expectations, we tested attendance for colposcopy during the colder months (influence of weather conditions and lack of infrastructure). Upon examining a map of the Eastern Cape region it became evident that visiting a colposcopy clinic could be time-consuming. Thus, patient attendance might be lowest from May through July, which is the winter season in South Africa.

Categorical data were analyzed using the Chi-square test, and continuous (numerical) data were analyzed using the Student's *t*-test[20]. All analyses were performed using SPSS v17. Categorical outcome variables included HIV data, which are categorical independent (certainty of HIV

positivity vs. patients with unknown status), the data regarding the grading and staging of cervical abnormalities (which are categorical independent groups with more than two categories), and the data regarding months of the year. Continuous data included age.

Results

The objective of this audit was to determine how many patients who received an abnormal Pap smear result attended at the colposcopy clinics at either Frere Hospital or Cecilia Makiwane Hospital. The audit revealed that a relatively low percentage of patients actually visited the colposcopy clinic following an abnormal Pap smear. From a total of 928 patients, only 54% attended colposcopy.

Because attendance at the colposcopy clinic was so low, we next examined the possible factors that underlie this phenomenon, including HIV status, age, the lesion's severity and CIN, and the month of attendance (i.e., month when the patient attended colposcopy). Data regarding these potential co-factors were available for 864 of the 928 patients, and analyzing these four factors yielded the following results.

HIV correlation

Of the 864 patients for whom HIV status was available, 131 (15.2%) were definitively confirmed as HIV-positive, and 35 (26.7%) of these 131 HIV-positive patients were non-attenders for a colposcopy. Interestingly, 73.3% of the 131 HIV-positive patients did return for a colposcopy, compared with only 44.5% (326 out of 733) of patients with unknown HIV status (Table 1).

Table 1: Association of HIV status and the percentage of HIV patients who returned to attend colposcopy

HIV Status	Total Number of Patients	Returned	Did Not Return
HIV-positive	131	96 (73.3%)	35 (26.7%)
HIV status unknown	733	326 (44.5%)	407 (55.5%)
Total:	864	422	442

The Pearson Chi-square value was 36.912 [df=1] ($p<0.001$). In contrast with our initial hypothesis, this finding suggests that HIV positivity has a positive influence on colposcopy attendance. Nevertheless, 733/864 (84.8%) of the patients had an unknown HIV status, (i.e., their status could be either negative or positive); therefore, we could not determine the actual number of HIV-negative patients, nor could we determine how many HIV-negative patients would have attended for colposcopy. Because of the indeterminate HIV status of these patients, we cannot draw clear conclusions regarding whether HIV status truly influences colposcopy attendance.

Age correlation

Among the 864 patients, 422 were non-attending and 442 attended colposcopy. In the group of 422 non-attending patients, age was known for 408 patients, and their mean (±SD) age was 43.64±14.5 years. In the attending group, age was known for 429, and their age was 44.49±14.0 years ($p=0.388$; Student's *t*-test for independent samples). Thus, age does not appear to play a role in whether patients attend colposcopy.

CIN staging and lesion grading

We created seven categories for lesion grading and CIN staging. We then assigned each patient to one of these categories, and determined the number and percentage of attending and non-attending patients in each category. A total of 842 patients were assigned to the six categories (not including the patients in the category "other carcinoma's" (**Table 2**.)

Table 2: Categories for staging and lesion formation (excluding the category "Other Ca.")

Diagnostic Category	Total Number of Patients	Non-attenders	Attenders
CIN II	290 (34.4%)	156 (53.8%)	134 (46.2%)
CIN III	344 (40.9%)	175 (50.9%)	169 (49.1%)
CIN III CA	37 (4.4%)	16 (43.2%)	21 (56.8%)
Adenocarcinoma	35 (4.2%)	13 (37.1%)	22 (62.9%)
Squamous-cell carcinoma	106 (12.6%)	43 (40.6%)	63 (59.4%)
Other Carcinoma's	30 (3.6%)	13 (43.3%)	17 (56.7%)
Total:	842 (100%)	416	426

Table 3: Distribution of non-attenders & attenders following an abnormal Pap smear

Month	Total number of patients	Non-attenders	Attenders
April	28	13 (46.4%)	15 (53.6%)
May	23	7 (30.4%)	16 (69.6%)
Jun	30	15 (50.0%)	15 (50.0%)
Jul	36	16 (44.4%)	20 (55.6%)
Aug	46	18 (39.1%)	28 (60.9%)
Sep	43	25 (58.1%)	18 (41.9%)
Oct	75	37 (49.3%)	38 (50.7%)
Nov	49	21 (42.9%)	28 (57.1%)
Dec	23	10 (43.5%)	13 (56.5%)
Total:	353	162	191

The Pearson Chi-square value was 8.953 [df=5] (p=0.111), indicating no significant difference among the six diagnostic categories with respect to the percentage of attending versus non-attending patients. Thus, CIN staging and lesion grading do not correlate with attendance behavior.

Time of year

Analysed data (nine months - April through December 2006) included 353 patients who returned for a colposcopy after receiving an abnormal Pap smear result; by month (**Table 3**).The Pearson Chi-square value was 6.488 [df=8] (p=0.593). Thus, the decision whether to attend a colposcopy following an abnormal Pap smear result is not correlated with the time of year.

Discussion

In its pre-cancerous stage, cervical cancer can be treated relatively easily and effectively. However, to be effective, the treatment must be performed when the abnormal cells which can be detected quite easily with a simple Pap smear are pre-cancerous. Our audit shows that this is not always the case in rural areas of the Eastern Cape, in which many women who receive an abnormal Pap smear result fail to attend their gynecology clinic for a colposcopy and follow-up care. Consequently, these patients do not receive adequate preventive treatment.

The outcome of this audit and the four co-factors that were analyzed does not explain the relatively high non-attendance rate. Specifically, our analysis revealed that neither, age, staging of the lesions, nor time of year directly influences whether a patient is likely to attend the clinic and seek treatment. Moreover, although HIV status appeared to play a role, the high number of patients for whom HIV status was unknown obscured our analysis. Nevertheless, with respect to HIV status, certain conclusions can still be drawn.

HIV has been linked to cervical cancer by two distinct mechanisms. First, HIV infection decreases the number of infection-fighting CD4-positive cells; this low CD4-positive cell count increases the patient's susceptibility to disease and increases the severity of the cervical lesion, thus facilitating the development of cervical cancer[21]. Second, cervical cancer is caused primarily by human papillomavirus (HPV), a sexually transmitted virus; therefore, both HIV and HPV infection can be considered primarily sexually transmitted diseases and are therefore correlated

with sexual behavior in general[22]. Because HIV infection and cervical cancer formation are linked (and have cross-influencing morbidity and mortality factors), HIV was considered as a factor that might negatively influence colposcopy attendance. Our audit revealed that in contrast with our *a prior* expectation, HIV-positive patients were more likely to attend for a colposcopy compared to HIV-unknown patients (given the caveat that data regarding HIV-negative status were not available). Nevertheless, although non-attendance is not influenced by HIV infection, these data still have value; for example, the higher attendance among HIV-positive patients could have resulted from increased health concerns and a more positive opinion of the healthcare facilities (due to prior experiences whilst being treated for HIV). This finding can be used to help develop preventive and educational programs designed to inform HIV-positive patients regarding the importance of treatment compliance and to evaluate patient care while treating both diseases. Although specific recommendations cannot be given based solely on the data obtained from this study, this issue clearly merits future attention, given the correlation between the two diseases and the effect on disease prognosis.

The Female Cancer Foundation (FCF) has the goal to educate patients regarding the interaction between sexually transmitted diseases and cervical cancer. This concept of simultaneous education and treatment should be implemented in the rural settings of other developing countries[23]. However, additional research is needed in order to evaluate their effectiveness in other low-income countries.

In our audit, age did not influence the overall attendance behavior. Therefore we can conclude that younger patients are not more likely to attend for colposcopy. However, we were unable to test for age-specific influences on attendance behavior. Therefore, with respect to age, prospective studies are needed in order to determine the attitude towards cervical cancer screening among young women in rural South Africa[24].

The grading of the lesions and cervical abnormalities also did not influence the decision to attend for colposcopy. Specifically, we found no significant difference between the patients with respect to the various stages and categories.

Our hypothesis that time of year influences attendance was not supported. One study found that environmental characteristics seem to have a limited influence on active travel in developing rural areas[25]. On the other hand, another study of HIV patients mentioned longer distances between towns and clinics as a barrier for women to seek medical care. Anyhow, providing easy access to screening and treatment is essential for motivating patients to seek follow-up screening and if needed treatment.

Ultimately, whether a patient will attend the clinic for treatment of a pre-cancerous cervical lesion depends on many factors, including socio-economic factors, co-morbidity, an understanding of disease prevention methods, emotional factors, and other relevant factors.

Because these factors can be much more labile in rural areas of a developing country, social and anthropological studies are needed in order to understand the medical help-seeking behavior of women in rural areas of Africa and to address issues such as poverty, low education, and physical barriers, all of which can prevent women from accessing health services[26].

Conversely, receiving treatment can influence the aforementioned factors. Given this reciprocal cycle, the FCF aims to diagnose and provide on-the-spot treatment in order to eliminate cervical cancer in the long run. The FCF uses the "See-and-Treat" method, in which a mobile team visits women in rural areas in order to provide on-the-spot VIA diagnostic screening; women who are diagnosed with an appropriate cervical intraepithelial neoplasia (CIN) lesion can receive immediate treatment, followed by cryotherapy[27]. Cryotherapy is acceptable, safe, and effective; in 2004, a systematic review of studies conducted in developing countries revealed that this treatment is ~90% effective at treating all CIN grade lesions [28].

The FCF trains local healthcare workers to use the See-and-Treat method, who then train other local healthcare workers[29]. A 2009 study examined the efficiency of such interventions and concluded that local healthcare workers can improve the outcome in underserved populations for certain health conditions[30]. Despite mixed levels of effectiveness when analyzed by clinical context, the intervention of local health workers had the

highest effectiveness for select disease prevention programs, including cervical cancer screening. Thus, the FCF's approach appears reliable with respect to cervical cancer screening, and local healthcare workers can address this disease.

Goel et al. recently reported that VIA is an extremely sensitive method for screening ectocervical lesions[31]. The authors also noted that VIA is extremely cost-effective, easy to use, and provides instant results. Moreover, the See-and-Treat method can be applied during the first visit.

Finally, a large population-based survey conducted in rural Southwestern China found that a single VIA screen could detect more than half of all CIN II cases, the majority of CIN III cases, and 100% of cervical cancer cases[32]. The study further stated that if multiple cervical cancer screenings are not feasible (either logistically or financially), performing a single VIA may be the most efficient screening strategy, thus supporting the FCF's approach in rural areas such as the Eastern Cape, where attendance for both colposcopy-based screening and treatment is extremely low, and identifying the reasons that underlie this non-attendance behavior is difficult. This approach can be the background for implementing future screening initiatives in the developing world[33].

It is important to understand the urgency caused by fatal diseases including cervical cancer and how such diseases perpetuate poverty in developing countries[34]. Thus, we must evaluate further the effectiveness and outcome of local initiatives and treatment programs, including the FCF's single-VIA program, which can complement colposcopy screening and treatments provided in fixed hospital settings[35]. The high non-attendance rate revealed by our study emphasizes the need for initiatives to provide more efficient screening and treatment. Therefore, we embrace the "See-and-Treat" approach advocated by the Female Cancer Foundation in rural South Africa.

Limitations of this study

As described in the Methods, our analysis of patient data did not allow for interpolation of the missing data. The missing data reflect uncertainty regarding disease manifestations (for example, with respect to the histology records) and the co-factors that can contribute to disease (e.g., incomplete HIV status).

A systematic approach should be used in these rural settings to interpolate missing data through predictive distributions; however, such an approach can be challenging when large-scale data are collected in the form of an audit.

Regarding the manner in which patients were informed and approached for referral and colposcopy, we were unable to ask the clinicians how this was performed, nor could we ask the patients whether (and how) this affected their decision to seek treatment. Finally, the quality of case management and referral by the clinical staff could not be tested.

Finally, rural clinics need a standardized method for evaluating patient contact and treatment, as well as computerized documentation methods in order to measure management progress and provide higher-quality patient care. Improved documentation methods, preserving both handwritten and computerized data, and communication with respect to patient data are also needed.

Other study methods should be used (questionnaire, surveys) when analyzing factors such as patient age or attendance. They might help identifying the factors that contribute to the decision to travel a long distance to the clinic for treatment.

Conclusions

After receiving a diagnosis of a potentially pre-cancerous cervical lesion, many women in rural South Africa do not seek a follow-up colposcopy and/or treatment. Given that attendance for conventional screening and treatment does not appear to depend on factors such as HIV status, age, lesion staging, or time of year, other factors health-related or otherwise might play a role. Identifying these factors will help improve the attendance rate and will decrease the number of pre-cancerous lesions that ultimately develop into cervical cancer. Regardless of which factors play a role in the morbidity and mortality of cervical cancer, prevention plays a key role in the management of this deadly yet easily prevented disease, and multidisciplinary approaches are

needed to implement effective prevention. For example, initiatives to improve both the knowledge of cervical abnormalities and treatment-seeking behavior in developing countries are needed. We therefore embrace the idea of using cost-effective mobile screening services such as the FCF's "See-and-Treat" method, which uses local healthcare providers to screen and treat cervical disease in conjunction with conventional hospital screening.

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Declaration of Interest

The author reports no declarations of interest

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