

## RESEARCH ARTICLE

# Cervical Precancerous Lesions and Cancer among Patients in the Gynaecology Outpatient Department at a Tertiary Hospital in South Africa

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### Abstract

**Background:** The purpose of this study was to determine proportional rates of cervical precancerous lesions and cancer, and associations with socio-demographic variables, HIV status, and CD4 cell count. **Materials and Methods:** A retrospective comparative study was conducted targeting the medical records of all women over age 18 that were diagnosed histologically through colposcopy with cervical precancerous lesions and cancer from 1 December 2011 to 30 November 2012. **Results:** A total of 313 patient records were used for data analysis. The average age was 39.1 (SD=2.04) years. More than a third (37.1%) of the patients had CIN III or cervical cancer. There was a significant association between age, CD4 cell count, HIV status, and cervical lesions ( $p < 0.05$ ). Age was found to be an influential predictor of cervical lesions (OR=0.67, 95% CI: 0.46-0.98). **Conclusions:** There exists an association between age and cervical lesions, with presentation of cervical precancerous lesions and cervical cancer at a younger age among HIV reactive patients. The National Guidelines should be brought in line with the National HIV Counseling and Testing Policy to offer Pap smears to all sexually active women that test HIV reactive during routine HIV Testing.

**Keywords:** Cervical precancerous lesions and cancer - CD4 cell count - HIV status - national guidelines - South Africa.

*Asian Pac J Cancer Prev*, 14 (8), 4903-4906

### Introduction

Cervical cancer (CC) is a leading cause of deaths among women worldwide. It is the third most commonly diagnosed cancer and the fourth leading cause of cancer deaths in females worldwide, accounting for 529,800 new cancer cases and 275,100 cancer deaths among females in 2008 (Jemal et al., 2011). More than 85% of these cases and deaths occur in developing countries. Worldwide, the highest incidence rates of CC are in Eastern, Western, and Southern Africa (Jemal et al., 2011).

In South Africa, CC is the second leading cause of death among women (Francis et al., 2011). According to the Cancer Association of South Africa (CANSA) (2000-2001), women have a lifetime risk of 1 in 35 of getting cancer of the cervix (CANSA, 2000-2001). Thus, CC among women in South Africa is an important Public Health concerns (Moodley et al., 2009).

According to the South African policy guideline on screening for cancer of the cervix to improve the health of a vulnerable group of the population, three free Papanicolaou (Pap) smears are offered, in a lifetime separated by ten years and starting at age 30 years of age. It is offered throughout South Africa's public health facilities (NDOH, 2000). Currently, according to annual internal

gynaecology audits conducted at the hospital on CC and precancerous lesions of the Cervix, most women above the age of 18 that are presenting with invasive cervical cancer (ICC) and precancerous lesions of the cervix, at the Gynaecology outpatient department (GOPD), are younger than expected (<40 years). This means that women are sexually active much earlier and infected with Human Papilloma Virus (HPV) infection, at very a young age which indicates that women should be screened earlier than 30 years through education on Pap smear services. The distribution of cervical precancerous lesions and CC among different age groups has not yet been adequately investigated. Therefore, the purpose of this study is to investigate cervical precancerous lesions and cancer of the cervix, among female patients, seen in the GOPD at a tertiary hospital in South Africa.

### Materials and Methods

#### Research design and settings

This was a retrospective comparative study was conducted, targeting the medical records of all women over the age of 18 that consulted the GOPD at Rahima Moosa Hospital from 1 December 2011 to 30 November 2012. The hospital is the main Academic Hospital of

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the West Rand, as well as one of the teaching hospitals of the University of the Witwatersrand, that provide tertiary level healthcare to women and children of the West Rand, Gauteng province. This hospital serves as the main referral hospital for Leratong hospital, a regional public healthcare hospital, Dr Yusuf Dadoo hospital, a primary level public healthcare hospital, and the Local municipal and district clinics that refer to all three hospitals. The West Rand consist primarily of the towns of Roodepoort, Krugersdorp, and Randfontein. Leratong is located in Roodepoort and Dr Yusuf Dadoo is located in Krugersdorp. Patients that were diagnosed with an abnormal Pap smear through routine cervical screening tests at any of the health facilities in the West Rand, were then referred to the GOPD for colposcopy, for confirmatory definitive diagnoses of a pre-cancerous cervical lesion such as CIN I, CIN II or CIN III. Women, who also tested HIV Reactive that participated in the National HIV Counseling and Testing (HCT) campaign, were also offered cervical screening tests, in line with the HCT Policy guidelines (NDOH, 2010).

#### Sampling and sample size

All the medical patient records of women above the age of 18 who visited the GOPD between 1 December 2011 to 30 November 2012 formed part of the study. Based on monthly Gynaecology Mortality and Morbidity statistics, it was estimated that information from  $\pm 4800$  patient records was collected in this study, during the study periods. According to the monthly Mortality and Morbidity statistics, the monthly abnormal Pap smears confirmed by Colposcopy results totaled to an average of  $\pm 25$  per month, giving a total of  $\pm 300$  over a twelve month period. This number was used to estimate the total number of Cervical disease case load, that include Cervical intra-epithelial neoplasia (CIN I, II, III) and CC. This number also constituted the sample size or working sample.

#### Inclusion and exclusion criteria

All patients above the age of 18 years that are visiting the GOPD of the hospital were included into the Study. All patients below the age of 18 and not visiting the GOPD of the hospital were excluded from the study.

#### Data collection

Data were collected from the GOPD and Colposcopy registry as well as personal patient medical records that correlate with the GOPD register. The Biological and Socio-demographical data were collected by the researcher, assisted by medical and nursing personnel, from official National Health Laboratory Service (NHLS) results sheets and official patient records. The register is the only official record of all GOPD visits on a daily basis, is the property of the Gauteng Health Department, and is maintained by the nursing personnel, employed in the GOPD. These do not require training in data collection, since they perform this function routinely in statistical processing for both weekly Gynaecological Mortality and Morbidity meetings, as well as the Gauteng Health Department.

#### Data analysis

Data were entered into a Microsoft Excel 2003 spreadsheet and imported to SPSS 17.0 for window version for analysis. The demographics and baseline outcome variables were summarized using descriptive summary measures: expressed as mean (standard deviation) for continuous variables, and percent for categorical variables. The chi-square test was used to find any associations between categorical variables. Binary logistic regression method was carried out to find significant predictor for Cervical lesions. All statistical tests were performed using two-sided tests at the 0.05 level of significance. P values less than 0.05 were considered to be statistically significant.

## Results

A total of 335 patient records were identified and accessed based on the GOPD and Colposcopy clinic registry, with a definitive NHLS Histology report,

**Table 1. Socio-Demographic Information of the Patients (n=313)**

Variables	Frequency	Percentage	
Age (years)	<30	55	17.6
	30-45	190	60.7
	$\geq 45$	68	21.7
Average age (SD)	39.06 (2.041)		
Marital status	Single	263	84
	Married	50	16
Racial Status	Black	269	85.9
	Non-Black	44	14.1
Employment Status	Employed	81	25.9
	Unemployed	232	74.1
Smoking Status	Smoking	216	69
	Non-smoking	97	31

**Table 2. Distribution of HIV Status and CD4 Cell Counts among the Patients (n=313)**

Variables	Frequency	Percentage	
HIV Status (n=313)	Reactive (Positive)	179	57.2
	Non-Reactive (Negative)	134	42.8
CD4 cell counts	<200	50	16.0
	200-350	52	16.6
	351-1000	74	23.6
	>1000	137	43.8

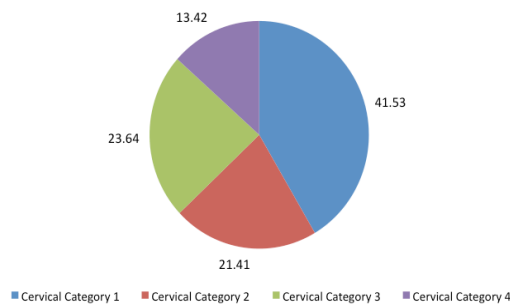
**Table 3. Association between Age, Marital Status, HIV Status, CD4 Cell Counts and Cervical Pre-Cancerous Lesions and Cervical Cancer**

Variables		Cervical Category				Pearson Chi-square	p value
		CIN			Cervical Cancer		
		I	II	III			
Age (years)	<30	28	13	13	1	26.97	<0.001
	30-45	77	44	49	20		
	>45	25	10	12	21		
Marital status	Single	108	55	66	27	23.37	<0.001
	Married	22	12	10	15		
HIV status	Reactive	64	46	47	19	10.45	0.015
	Non-reactive	66	21	27	23		
CD4 cell counts	<200	17	17	13	3	18.1	0.034
	200-350	15	11	18	8		
	350-1000	32	18	16	8		
	>1000	66	21	27	23		

**Table 4. Backward Stepwise (Likelihood ratio) Logistic Regression Output for CINIII and CC**

Independent variables	B	S.E.	Wald	p value	Odds Ratio (OR)	95%CI for OR	
						Lower	Upper
Age Category*		8.192	0.017				
30-45 years	0.537	0.351	2.346	0.126	1.711	0.861	3.401
>45 years	1.144	0.407	7.922	0.005	3.141	1.416	6.968
HIV Status	-0.019	0.321	0.004	0.953	0.981	0.523	1.841
cd4 Cell counts**		5.618	0.06				
<200	-0.055	0.396	0.02	0.889	0.946	0.436	2.055
200-500	0.787	0.377	4.366	0.037	2.198	1.05	4.599

\*<30 years as reference group, \*\*> 500 as reference group. Variable(s) entered on step 1: Age Category, HIV Status, cd4 cell counts



**Figure 1. Distribution of Cervical Lesions among the Patients Seen at the Hospital**

diagnosing either CIN I, CIN II, CIN III or CC. Out of 335 records, 22 patient records had missing data such as HIV status and/or CD4 Cell count. The Socio-demographic data revealed that average age of the patients was 39.06 years (SD=2.04) as more than three quarters (78.3%) of them were less than 45 years old. Majority of the patients were single (84%), Black (86%), unemployed (74%), and smoker (69%) (Table 1). Regarding, the distribution of cervical lesions, more than a third of the patients (37.06%) had CIN III or CC (Figure 1).

Regarding HIV status, more than half (57%) were HIV positive. Results also indicated that about a third of the HIV positive patients, their CD4 cell counts were 350 or less (Table 2). Results indicated that cervical precancerous lesions and CC was significantly associated with age of the patients, marital status, HIV status, and CD4 cell counts ( $p < 0.05$ ) (Table 3). Binary Logistic Regression was performed to predict CC (CIN 3 and CC) as CC and CIN 1 and CIN 2 as non-cancer) on those variables that had significant association from bi-variate analysis. According to Table 4, age and CD4 cell counts were predictors.

## Discussion

The present study found that 63% of the patients fall in the CIN I and CIN II cervical lesion category. A possible explanation for this proportional rate variance among the various Cervical lesions is the fact that some CIN II lesions might regress to CIN I lesions and that some CIN I lesions might regress to normal (Kruger and Botha 2008; Levisohn et al., 2008; Ho et al., 2011). This regression is dependent on the competency of the patient's immune system and also in the case of HIV Reactive patients; the sooner the patient is placed on HAART, the higher the possibility of CIN regression and the reduction in CIN prevalence among HIV Reactive patients (Levisohn et al., 2008; Memiah et al., 2012). Another possible explanation

could be that factors associated with progression from CIN II and CIN III to invasive cancer is not well understood, and that most CIN II and CIN III do not always progress to cancer (Wentzensen et al., 2013).

The study reveals a mean age of 39 years for the entire study population, in whom cervical lesions was diagnosed definitively through histological techniques. This finding is comparable with other studies. For example, a Center for Disease Control (CDC) epidemiological study found that 78% of the CC cases were diagnosed in women aged 30-39 (Benard et al., 2012). Moyer (2012) reported that CC most commonly occurs in women age 35-55 years. A Brazilian study conducted to determine the Prevalence of human papillomavirus from patients with cervical pre-malignant and malignant lesions found the mean age of CC among these women was 47.3 years (Fernandes et al., 2010).

The present study found significant association with age of the patients. An Egyptian study concluded that HPVs infection was more pronounced in younger age women. Gupta et al. (2008) concluded that the peak age incidence for squamous intraepithelial lesions (SILs) in the 30-39 age group. Contrary to these findings, an Indian study conducted among underserved women found no significant difference among women with or without precancerous lesions or CC lesions among women below 30 years of age with those women above 30 years of age (Chankapa et al., 2011).

This study found significant association between marital status and cervical pre-cancerous lesions or CC. This is a contradictory finding from that of a Korean study. The Korean study reported that cancer mortality among Korean women between 1998 and 2009 was lower in married women than unmarried women in all age groups, and the degree of difference did not change over time (Kim et al., 2012). Another possibility, although not investigated in this study, could be the fact that a large proportion of the participants, due to their single marital status, may be involved in multiple sexual partner relationships. A Tanzanian study found that single marital status and number of lifetime sex partners were risk factors, significantly associated with SIL (Obure et al., 2009).

The CD4 Cell count and HIV status were analyzed individually and in conjunction with the Socio-demographic variables. Analyzing the CD4 cell count individually among HIV Reactive patients, the study reveal an overall mean CD4 Cell count was 337 indicating immune system compromization in terms of CD4 reference levels as well as 350 indicating severe immune compromization in terms

both National South African ART Treatment guidelines and WHO ART recommendations (NDOH, 2010; WHO 2010). The study also reveals majority of HIV Reactive patients have a CD4 cell count <500. This analysis alone poses some public health challenges, for example what percentage of patients, if any is on either ART or HAART while being managed clinically for cervical lesions. This challenge hopefully can be addressed in future prospective studies.

In the present study, CD4 cell count was associated with cervical pre cancer lesions and CC, in line with other studies conducted in USA and Kenya. The USA study reported that among CIN II patients CD4 Cell counts were less than 350 and the Kenyan study reported median counts of 239 among women diagnosed with Squamous Intra-epithelial Lesion (McKenzie et al., 2011; Keller et al., 2012). A recent South African study concluded that there is an increasing risk for cervical lesion progression in women with CD4 Cell counts below 500 (Omar et al., 2011). The same study found that HAART reduce the risk of cervical progression, clearly emphasizing the role of a low CD4 cell count in cervical progression.

HIV status and cervical pre cancer lesions and CC were significantly associated which is a confirmatory finding. Interestingly, a case-control study, conducted by Moodley et al. (2006), to determine the relationship between HIV and pre-neoplastic and neoplastic lesions of the cervix, among Capetonian women in South Africa found that HIV positive women with CC were 6 years younger than those women that were HIV negative with a median age of 40 years and 46 years for HIV positive and HIV negative women respectively.

This was a retrospective study so it was prone to missing data. We had a large sample size which minimized this bias. The full impact of HPV and its complications in cervical disease pathogenesis, although established in other studies, could not be fully realized in this study.

In conclusions, more than a third of the patients were in CIN III or CC stage. There was a significant relationship between age, race, marital status, HIV status, CD4 cell counts with the progression of Cervical Intraepithelial lesions. The National Guidelines should be brought in line with the National HIV Counselling and Testing Policy to offer Pap smears to all sexually active women that test HIV reactive during routine HIV Testing.

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