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## Does screening for cervical intra-epithelial neoplasm in developing countries prevent invasive cervical cancer?

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### Summary

In a bid to evaluate the practical relevance of screening for cervical intraepithelial neoplasia (CIN) in reducing the incidence of invasive cancer in Nigeria, we performed a comparative study of CIN and invasive carcinoma in Ibadan, Nigeria over a period of 8 and 16 years respectively. 4.5% of patients with invasive cervical cancer were under the age of 30 years. It peaked at 28% in the age group 41-50 years. In comparison, <3% of patients with CIN were below 20 years of age while it had the highest incidence of 37%, 34% and 36% respectively in age 40 years and below. The mean age for CIN was  $39.6 \pm 9.6$  (SD) years compared to  $51.3 \pm 11.1$  (SD) years for invasive cervical cancer ( $p < 0.01$ ). There was a 10 year interval between the onset and peak age incidence of invasive cancer and CIN respectively, even though there was an overlap of cases from the third decade. We therefore suggest a combined approach of public education to encourage early presentation and provision of health service outlets for cervical cancer screening in Nigeria to reduce the burden of cervical cancer.

**Keywords:** Cervical, intraepithelial, neoplasia, carcinoma, cancer

### Résumé

Dans un désir d'évaluer l'importance pratique de scanner le néoplasme intraépithéliale du cervicale (CIN) pour réduire l'incidence invasive du cancer au Nigéria. Nous avons effectué une étude comparative du CIN et le carcinome invasive dans la ville d'Ibadan, au Nigeria durant une période de 8 à 16 ans respectivement. 4.5% des patients ayant le cancer cervical étaient age de moins de 30 ans. Un peak de 28% était observé dans ce groupe d'age de 31-50ans. En comparaison, moins de 3% des patients ayant le CIN était agés de moins de 20 ans. Il avait la plus grande incidence de 37%, 34% et 36% à l'age de 40 ans et en dessous respectivement. La moyenne d'age pour les CIN était de  $39.6 \pm 9.6$  ans comparé à  $51.3 \pm 11.1$  SD ans pour ceux ayant le cancer cervical ( $P < 0.01$ ). Il avait un interval de différence 10 ans entre le début et le sommet d'age du cancer cervical et de CIN, Bienque il avait un retard des cas la 3 ieme dizaine. Nous avons ainsi suggérer une approche combinée d'éducation publique pour encourager une prevention précoce et la provision des centres des sions de santé pour contrôler le cancer cervical afin de réduire la souffrance du cancer cervical au Nigéria.

### Introduction

Cervical cancer is an important health problem of women in Nigeria and other developing countries as it is the most common cancer in women and the second most common cancer in women world wide [1-2]. It remains a major cause of

mortality in women in developing countries despite the fact that it is now a preventable disease [2-3].

The dramatic decline in the occurrence of invasive cancer of the cervix in developed countries is attributable to two factors. Firstly, the recognition of the pre-invasive pathological condition of the cervical epithelium referred to in the past as dysplasia and secondly, the development of an effective screening test that can identify this pre-invasive neoplastic condition in asymptomatic women [4]. In developed countries, the employment of modern treatment modalities such as laser vapourisation/conisation and large loop excision of the transformation zone (LLETZ/LEEP) in eradicating the lesion even when seen in the premalignant stages has a success rate exceeding 95% [4].

However despite these advances in knowledge globally, no developing country has succeeded in establishing a successful population-screening programme or has provided a reliable programme for treatment of the intraepithelial neoplasia. The result is a continuation of the scourge of cervical cancer with presentation at advanced stages, distressing morbidity and continued mortality.

Studies among Caucasians suggest that the progression from dysplasia through carcinoma in-situ to invasive cancer occurs over a period of 10- 20 years with dysplasia being common in the age range of 20-30 years, carcinoma in-situ between 30-40 years and invasive cancer in the 40-50 years age group [4-5]. To the best of our knowledge there has been no study in Nigeria to establish the practical relevance of screening for cervical intraepithelial neoplasia (CIN) in reducing the incidence of invasive cancer.

We have therefore undertaken this comparative study of CIN and invasive cancer in Ibadan, Nigeria by reviewing the demographic characteristics of Nigerians with CIN and relate these to those of patients with invasive cervical cancer with a view to establishing a causal relationship between CIN and invasive cervical cancer.

### Materials and methods

The study is a comparative retrospective review of the medical records of all patients with cervical intraepithelial neoplasia (CIN) seen at the University College Hospital between January 1, 1989 and 31<sup>st</sup> December 1996 (8 years). This is compared with our previous demographic data of 16 years on invasive cervical cancer by Adewole *et al* [6]. This is with a view to studying a possible relationship between CIN and cervical cancer in our environment.

Information was obtained from the cancer registry and cytology register in this hospital and data were meticulously scrutinized to avoid duplication. Important variables recorded included year of diagnosis, age and parity of the patients. The information was coded into a computer using the EPI-INFO 283 (CDC/WHO, 1996). Frequency tables were generated, and



means and standard deviations were computed. The mean age of the groups were compared using analysis of variance (ANOVA) and test of proportion was performed using chi-square. The level of statistical significance was fixed at  $P < 0.05$ .

### Results

There were 314 cases of CIN out of a total of 2643 smears within the period of study. Thus, overall CIN rate was 11.9%. There were 1014 cases of invasive carcinoma of the cervix. Figure 1 shows that the majority of the patients (68.8%) had CIN I and only about 10% had CIN III.

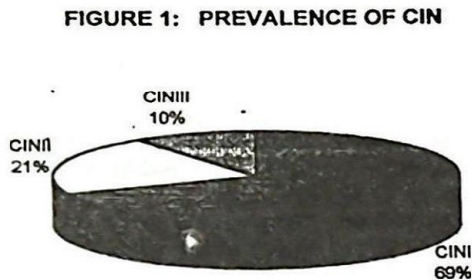


Fig. 1:

Figure 2 shows the age incidence by grades of CIN and cervical carcinoma. 4.5% of patients with invasive cervical cancer were under the age of 30 years. It was found in 48% and 47.5% of patients in the age groups 31-50 and above 50 years respectively.

In comparison, CIN I, II and III was found in 20%, 16% and 16% of the patients below the age of 30 years, 68%, 58% and 63% of the patients in the age group of 31-50 years and above the age of 50 years it was found in 14%, 26% and 21% respectively. (fig 2).

**FIGURE 2 PREVALENCE OF CIN and CERVICAL CANCER**

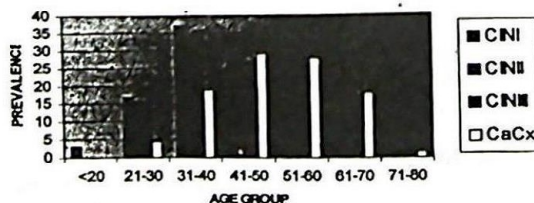


Fig. 2:

Fig. 2 also shows that the peak age incidence of invasive cervical carcinoma was 41-50 years as against 31-40 years for CIN.

The mean age of patients with CIN was  $39.6 \pm 9.6$  years, while the mean age of patients with cervical carcinoma was  $51.3 \pm 11.9$  years as shown in table I. The difference between the mean ages of patients in the two groups was significant ( $P < 0.01$ ). There was no significant difference in the

ages of patients with CIN but the age was significantly different for different stages of cervical carcinoma, suggesting an increase in age with increasing stage of the disease.

**Table 1: Mean age of patients with CIN and cervical cancer**

	Frequency	Mean age/ yrs $\pm$ St. dev.
<i>CIN</i>		
Grade I	215	$38.7 \pm 8.7$
Grade II	67	$41.1 \pm 10.6$
Grade III	31	$42.04 \pm 12.5$
Overall	314	$39.58 \pm 9.6$
<i>Cervical Cancer</i>		
Stage I	88	$46.6 \pm 10.9^*$
stage II	217	$50.7 \pm 12.5^*$
Stage III	437	$54.0 \pm 12.0^*$
Stage IV	272	$54.3 \pm 11.9^*$
Overall	1014	$51.3 \pm 11.9$

\* $P < 0.05$

### Discussion

Cervical cancer remains a major reproductive health problem in Nigeria as reflected by the result of this study. There was a ten - year time lag between the onset of invasive cancer and CIN as demonstrated by a preponderance of CIN in the fourth decade as against a peak occurrence of invasive cancer of cervix in the fifth decade of life. This suggests that the disease probably progress from a dysplastic stage to invasive cancer over a 10-year period. This is similar to the findings amongst Caucasians in prospective study of over 500 women with cervical intraepithelial lesions [5].

Furthermore, there was an overlap of patients with CIN and invasive cervical carcinoma after the age of 20 years. Babarinsa *et al* [2] also found that the age - specific incidence is falling in the older groups, but rising in the younger groups. This probably reflects an earlier age at acquisition of human papilloma virus (HPV) infection. However, the peak age incidence of cervical carcinoma is similar to the findings of previous workers [7-12 About 30% of the patients had CIN II and III. This will require treatment techniques such as cold coagulation, cryotherapy, laser vapourisation and large loop excision of the transformation zone. It will be necessary to equip the referral centers with the facilities for treating these lesions. It is well accepted that screening should begin once a woman becomes sexually active because of the implication of coitus in the aetiology of the disease. This study suggests that screening should commence on or before 20 years of age which agrees with the findings of the Nigeria Demographic and health survey that 50% of all women are married before the age of 20 years and have high rate of premarital sex [13].

Subsequently, screening should be within ten years (peak incidence of CIN in the fourth decade of life) and screening should reasonably stop by 70 years. This compare favourably with the programme in the United States of starting at age 20 with annual pap test and pelvic examination and less frequently after three or more consecutive normal examinations. It is however, slightly different from the Scandinavian norm of starting at about the age of 25-35 years with repetition of the smear at 5-yearly intervals and upper limit of 60 years [14].



The findings of this study are in agreement with the recommendation of the World Health Organization that once a lifetime modified screening programme for developing countries at about the age of 40 years [15]. The mean age for CIN in this study was 39.6 years. It has been shown that a single cervical smear for all women in their fifth decade will reduce the incidence of invasive cervical cancer by 25% [16] and two tests per lifetime will reduce the incidence by 40%-50% [17]. Notwithstanding the shortcomings of this approach, it would be a good starting point and with improved infrastructure funding, a programme for screening from the second decade will be embarked upon until a more ideal programme is established.

It is known that the use and accuracy of the Pap smear declines with age, due to inadequate sampling of receding transforming zones and overdiagnosis of atrophy related changes. Thus colposcopy with biopsy in older women might define a small subset of patients who remain at appreciable risk and could benefit from close surveillance or definitive treatment.

In conclusion, the result of this study may be useful in formulating policies towards establishing a successful population-screening programme and thereby designing a reliable programme for the treatment of the intraepithelial neoplasias.

Further longitudinal studies of CIN and invasive cervical cancer may improve the quality of such programmes in reducing the incidence of invasive cervical carcinoma in our environment.

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