PREVALENCE OF SQUAMOUS CELL CARCINOMA AMONG CERVICAL CANCER PATIENTS IN IGBOS OF NIGERIA

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ABSTRACT

The aim of this study is to determine the prevalence of squamous cell carcinoma among the Igbos in Nigeria and to assess the relative associations of factors like age and parity on the disease. Reports on 206 histologically diagnosed cervical cancer cases were reviewed. The tissue blocks of these cases were also retrieved and sectioned at 5µm with rotary microtome. They were then stained with hematoxylin and eosin techniques for general tissue architecture and diagnosis. The stained slides were then viewed and confirmed under high power microscope. Of this number, 125 (60.5%) had squamous cell carcinoma and some infiltration of eosinophils in some of the stroma adjacent to the tumour cells. Prime clinical findings included irregular vaginal bleeding, vaginal discharge, lower abdominal pain and post coital bleeding. The mean age of presentation was 62±6.4 years. Age and parity of the patients appeared to be significantly associated with prevalence of the disease. Early detection and prompt treatment of cervical cancer patients is recommended in order to reduce the associated and ever increasing rate of mortality and morbidity.

Key Words: Squamous Cell Carcinoma, Cervical Cancer, Igbos, Nigeria.

INTRODUCTION

Cervical cancer is an important public health problem. It is the most common gynaecological malignant neoplasm all over the world (Cannistra and Niloff, 1996; Benedet et al., 2000). According to recent data, an estimated 500,000 new cases occurs annually world wide, with the vast majority in developing countries (Thomas et al., 2002). Over 80% of the estimated 321,000 deaths which occur annually due to cervical cancer also occur in these countries. In Nigeria, it is the second commonest female cancer, and the age-adjusted incidence rate is approximately 24.1 per 100,000 from Ibadan Cancer Registry data (1998-1999). This is probably an under estimation as there is general under reporting of cancer cases. In general, women of low socio-economic status have higher rates (Thomas et al., 2002).

Cervical cancer is a potentially preventable disease. It is therefore important to be aware of the risk factors, screening techniques and available diagnostic options with special attention to the management of the pre-invasive disease (Cannista and Niloff, 1965). The risk factors include women with multiple sex partners, early age of first intercourse (Christopherson and Parker, 1965), history of venereal disease, (Kessfer, 1976), women whose male partner have multiple partners (Gendershot,1983; Martin,1967), association with human papilloma (Walboomer et al., 1990; Luesley et al., 1994), sexually transmitted virus, and smoking (Winklestein, 1990; Luesley et al, 1994).

Cervical cancer is associated with a broad age range (Barber, 1988). In contrast, cervical intraepithelial neoplasia (CIN), which are the precursors of invasive disease, frequently occur in younger women, often under 35 years of age. The observation that the precursor lesions occur at a younger age than does invasive disease is consistent with the notion that the malignant transformation of squamous epithelial cells requires a longer latency period.

Significant decline in the prevalence and mortality of cervical cancer have been noted in the last 20 years, particularly in advanced areas of the world where screening programmes are better organized. Accessibility to treatment, early detection, reduction in parity, sexual behavioral change and awareness has contributed to its decline (Martin, 1967; Dickinson, 1975). Unfortunately, there has been no significant change in most developing countries like Nigeria. This is because the risk factors are still prevalent and the awareness as well as the huge material and human resources required for mass screening are lacking.
Diagnosis of cervical carcinoma depends on a high index of suspicion. However prime clinical findings may include irregular vaginal bleeding, vaginal discharge, lower abdominal pains and post-coital bleeding. This study is therefore aimed at determining the prevalence of squamous cell carcinoma among the Igbos with cervical cancer and to assess the relative associations of such factors as age and parity on the disease.

MATERIALS AND METHOD

A total of 206 cervical histopathology reports on surgical specimen obtained from patients of the Igbo ethnic group of Nigeria, between January 2007 and December 2010 were reviewed. The tissue blocks for these reports were also retrieved for the study. The surgical specimens with accompanying histopathological forms were obtained from 40 hospitals spread across the five states of South Eastern Nigeria. The reports on specimen taken from patients at National Orthopaedic Hospital Enugu, venue of the study, were excluded in order to demonstrate the true geographical pattern.

Each specimen was properly labeled with name, age, ethnic group, address of hospital, date of operation, and the referring doctor. Other data obtained from each patient’s histopathological form included clinical diagnosis, complaints and duration, clinical signs, parity and last menstrual period (LPM).

The already processed paraffin wax blocks were sectioned at 5µm with rotary microtome and the sections were stained with haematoxylin and eosin techniques for general tissue architecture and diagnosis. The stained slides were then viewed and confirmed under high power microscope.

RESULTS

The patient’s ages grouped into six age grades, ranged from 30-78 years and the age and cervical cancer occurrence within these years is shown in table 1.

The mean age at presentation was 62±6.4 years. Sixty-five percent of the patients were aged 50-69 years. The highest patient frequency was in the 60-69 age bracket group, while the least patient frequency was in the 30-39 age group. The distribution pattern shows a steady increase in the yearly occurrence of the disease as seen in table 2.

None of the cervical cancer patients was nulliparous. Nineteen and half percent (19.5%) had 1-4 pregnancies, 45.0% had 5-8 pregnancies, while 35.5% delivered 9 or more children. Eighty and half percent (80.5%) of the cervical cancer patients were grand multipara as seen in table 3.

A relationship between parity and the incidence of the disease may exist. Sixty percent (124) of the patients presented with a history of irregular vaginal bleeding alone, while 72% (148) presented with a history of irregular vaginal bleeding and post coital bleeding. Vaginal bleeding was therefore a major significant clinical finding (P≤0.05). Thirty (30) of the patients (15%) presented with vaginal discharge alone as shown in table 4. Squamous cell carcinoma was seen in a total of 125 cases (60.5%). Some showed infiltration of eosinophils in the stroma adjacent to the tumor cells. The tumour was composed of pleomorphic squame cells with eosinophilic cytoplasm and prominent nucleoli. Numerous cell nests and inflammatory cells abound.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30-39</td>
<td>9</td>
<td>4.5</td>
</tr>
<tr>
<td>40-49</td>
<td>22</td>
<td>10.5</td>
</tr>
<tr>
<td>50-59</td>
<td>61</td>
<td>29.5</td>
</tr>
<tr>
<td>60-69</td>
<td>73</td>
<td>35.5</td>
</tr>
<tr>
<td>70-79</td>
<td>41</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>206</td>
<td>100%</td>
</tr>
</tbody>
</table>
Table 2: Yearly Occurrence of Disease

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>30</td>
</tr>
<tr>
<td>2008</td>
<td>42</td>
</tr>
<tr>
<td>2009</td>
<td>68</td>
</tr>
<tr>
<td>2010</td>
<td>66</td>
</tr>
</tbody>
</table>

Table 3: Pregnancy distribution among the patients

<table>
<thead>
<tr>
<th>Parity group</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>40</td>
<td>19.5</td>
</tr>
<tr>
<td>5-8</td>
<td>93</td>
<td>45.0</td>
</tr>
<tr>
<td>9 or more</td>
<td>73</td>
<td>35.5</td>
</tr>
</tbody>
</table>

Table 4: Clinical findings among the patients

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>Total N= 206</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregular vaginal bleeding</td>
<td>124</td>
<td>60</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Lower Abdominal pains</td>
<td>28</td>
<td>13</td>
</tr>
<tr>
<td>Post coital bleeding</td>
<td>24</td>
<td>12</td>
</tr>
</tbody>
</table>

Figure 1: Photomicrograph of Squamous Cell Carcinoma of uterine cervix showing cell nests and epithelial cancer cell infiltration with skeletal stromal elements (Mag. x500; H & E)

DISCUSSION

Most of the cases of cervical cancer were seen in the peri-menopausal or post-menopausal patients. According to Edington and Gilles (1969), peri-menopausal women are frequently affected by cervical carcinoma in the tropics (Edington and Gilles, 1969). The study by Onuigbo (1976) among Nigerian Igbo women with cervical cancer revealed that about seventy percent of them were peri-menopausal.
Cervical Cancer is the second commonest malignancy seen in females in Nigeria and East Africa after breast cancer (Armon and Missalek, 1978). It is therefore of national importance as the mortality from the disease is appalling (Armon and Missalek, 1970). The age of presentation of cervical carcinoma in this study was in the sixth decade of life, about 20 years above the age reported in advanced countries like USA (Benedet et al., 2000, Liu et al., 2001).

Most patients present too late at the hospital for curative therapy as the facilities for early screening and detection are grossly inadequate. The resources used in carrying out the hysterectomies in patients with the attendant high mortality may be better channeled to the preventive stages of the disease. The high incidence rate and the late presentation of the disease emphasize the importance of the tumour in Nigeria (Onuigbo, 1976).

The age of the patient was given in 200 (97.1%) of the histopathological reports. All histopathological forms must be filled correctly and must contain the patients’ age and other clinical data as contained in the form. Errors in omitting the age or giving a wrong age will definitely affect future screening programmes. Future screening programmes and awareness campaigns should include all girls above 20 years since the disease is beginning to appear in much younger women less than 30 years (La Vecchia et al, 1984; Macleod et al, 1994; Dickinson, 1975; Ibeachum, 1978). The steady increase in the yearly occurrence of the disease from 2007-2010 is worrisome. The number of cancer patients seen in 2007 had doubled by 2010 (Table 3). In all probability, with increasing morbidity and mortality, there is decreasing workforce and productivity. Hence more awareness should be created by the relevant government agencies and more screening centers established to check the rising trend.

The finding that none of the cervical cancer patients in the study was nulliparous is very significant and agrees with earlier studies (Guido et al., 1974). The disease is very rare in nuns. Parity may therefore reflect the coital etiological factors associated with squamous cell carcinoma. This study reveals that eighty and half (80.5%) of the Igbos with cervical cancer were grand multiparous. It is known that high parity increases the risk of cervical cancer (Hinkula et al., 2004), especially among human papilloma virus (HPV)-positive women (Eluf –Neto et al., 1994). The relative risk of cervical cancer among women with five or more births varied from 3.8 (in squamous cell carcinoma) (Munoz et al., 2002) to 4.4 (Parazzini et al., 1989) compared with nulliparous or primiparous women (Brinton et al., 1989). It is therefore not surprising that cervical cancer may be common among women in our locality.

There are several pregnancy-induced cervical changes, which may predispose to malignant transformations. Multiparity may increase the risk of cervical cancer by maintaining the transformation zone on the ectocervical region (Brinton et al., 1989). Moreover, the number of squamous metaplastic cells in the transformation zone increases during pregnancy (Munoz et al., 2002). In their immature phase of development, the metaplastic cells are most susceptible to HPV infection and possibly later to progression to cervical cancer. The metaplastic transformation zone in the ectocervix of a grand multiparous will repeatedly be exposed to carcinogenic agents. For this reason, multiparity may intensify the actions of carcinogenic infectious agents (Nair and Pillai, 1992).

The percentage of the squamous cell carcinoma in the study (60.5%) is smaller than that quoted by other authors elsewhere (Ibeachum, 1978). In fact, the possibility exists that by using the sulphosalicyclic silver bath (three-5-bath) described by Ibeachum (1982) and later employed by him to demonstrated epithelial intercellular bridges in paraffin sections, some if not most of the undifferentiated carcinomas might turn out to be differentiated and of the squamous cell types (Ibeachum, 1982; Ibeachum 1978). A variety of stromal reactions are associated with invasive carcinoma. The most common responses are an infiltrate of inflammatory cells, especially mononuclear cells such as lymphocytes and plasma cells. Eosinophilic leukocytes are seen among the inflammatory cells but are seldom the major constituents.

In this study, the observation of eosinophil infiltration in some cervical squamous cell carcinoma is similar to that found by Lasersolin et al, (1964), who also noted an association with large pleomorphic cells. There are two likely explanations for eosinophilia associated with these cervical carcinomas. The carcinoma cells themselves may directly manufacture eosinotactic and eosinopoietic factors (Bostrum and Williams 1981). This mechanism would be analogues to the occasional production and secretion of ectopic hormones (gonadotrophins, erythropoietin), adencorticotropicin, parathormone, etc) by some tumours of non endocrine origin. Alternatively, the eosinophilia may result indirectly from immunologic
reactions of inflammatory lymphoid cells and mast cells with antigens of the carcinoma cells. While it seems probable that the eosinophils represent a specific reaction to the tumour cells, there is some evidence that these cases have higher frequency of metastases (Lowe et al, 1981) than in other squamous cell types. The prognostic significance of tissue eosinophilia therefore needs further studies.

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**AUTHOR(S) CONTRIBUTION**

Ngwogu K.O, Ndubuka G.I.N, Ngwogu A.C, contributed to the successful completion of this study. Their career background played important roles.