Original Research

A Review of Vulvar and Vaginal Cancers in Ibadan, Nigeria

Clement A. Okolo, MBBS, FMCPath;[1] M. Olatokunboh Odubanjo, MBBS, FMCPath;[1]*
Olutosin A. Awolude, MBBS, FMCOG;[2] Effiong EU Akang, MBBS, FMCPath, FWACP[1]

[1] *Department of Pathology, University College Hospital, Ibadan, Nigeria*
[2] *Department of Obstetrics and Gynecology, University College Hospital, Ibadan, Nigeria*

The objectives of this study are to give an update on the previous studies on vulvar and vaginal cancers from the University College Hospital (UCH), Ibadan, Nigeria, to elucidate any changes in pattern, and to enumerate some of the factors affecting the management of these cancers at the UCH today. All the cases of cancer of the vulva and vagina seen at the UCH between January 1981 and December 2008 were reviewed and re-classified according to the World Health Organization (WHO) histological classification of 2004. The results are as follows: Vaginal and vulvar cancers were the 4th (1.4%) and 5th (1.2%) most common of the 5913 gynecological cancers seen. The mean age was 49.7 years. Squamous cell carcinoma (SCC) was the most common histological type. Notably, vulvar cancer is more common than vaginal cancer in the US and the UK and this opposes our findings. We studied time periods before and after the year 2000, and found vaginal cancer to be more common before and vulvar cancer after the year 2000. We suggest that this may be related to the introduction of the FIGO guidelines in 2000. We conclude that it is important to strictly adhere to the FIGO guidelines in determining the primary site of origin of these cancers in patients with advanced local disease as this distinction has implications for clinical management.
[N A J Med Sci. 2013;6(2):76-81. **DOI:** *10.7156/najms.2013.0602076]*

Key Words: *vulvar, vaginal, cancer, squamous cell carcinoma, Ibadan, Nigeria*

INTRODUCTION

This study aims to describe the histopathological pattern of vulvar and vaginal cancers at the University College Hospital (UCH), Ibadan. The last study of vulvar and vaginal cancers carried out at the UCH was published in 1998.[1] This present study seeks to give an update, to elucidate any changes in pattern, and to enumerate some of the factors affecting the management of these cancers at the UCH today.

Persistent Human papillomavirus (HPV) infection is a notable risk factor for both vulvar and vaginal cancers. In the United States, it has been reported that 40% of vulvar [2] and vaginal cancers[3] could be attributed to Human Papillomavirus (HPV), and HPV type 16 (HPV-16) was detected in 50-64% of high-grade vaginal intraepithelial lesions (VAIN).[2]

Worldwide, vulvar and vaginal cancers are rare.[4,5] Independent reports from Nigeria, United Kingdom and the United States show these cancers to be rare.[6,7,8] In the United States, vulvar cancer accounts for 0.6% of all cancers in women,[3] and vaginal cancer for 0.3% of all invasive cancers among women.[2] Majority of these cancers occur in developing countries.[6] It is reported that 60% of vulvar cancers and 68% of vaginal cancers occur in developing countries.[6]

Thomas et al[9] described the prevalence of HPV infection in Nigerian women as well as the distribution of various HPV subtypes among women with normal and abnormal findings on cytology or Visual inspection with acetic acid. HPV 16 and 35 were the most common high-risk HPV types, and HPV 42 was the most common low risk type.[9] There is need for further epidemiological studies on the role of HPV in various cancers in our environment, as well as the distribution of the various subtypes in these cancers.

Worldwide and in the US, there has been profound excitement and concern surrounding the HPV vaccine. The excitement derives from the potential of the vaccine to reduce the burden of anogenital cancers in countries that have no screening infrastructure. There are concerns however, that if vaccine uptake is lower in those groups at highest risk of developing cervical cancer, current racial/ethnic or geographic disparities could increase.[6] For Nigerians, the HPV vaccine may be useful in reducing the burden of disease provided we can afford them and the same HPV subtypes (mostly HPV 16 and 18) targeted by these vaccines are important causes of cancer in Nigeria.

Received 03/15/2013; Revised 04/16/2013; Accepted 04/26/2013
***Corresponding Author:** Dept of Pathology, University College Hospital, Ibadan, Nigeria. (Email: todubanjo2002@yahoo.com)

METHODS

Details of all histologically confirmed cases of cancer of the vulva and vagina seen at the University College Hospital (UCH), Ibadan between January 1981 and December 2008 were obtained from the records of the Ibadan Cancer Registry. All the cases were re-classified according to the WHO histological classification of the tumors of the vagina and the classification of the tumors of the vulva published in 2004.[4,5] The data obtained was analyzed using SPSS version 15.0.

RESULTS

A total of 162 cases of vulvar and vaginal cancers were found in the records of the Ibadan Cancer Registry for the period from January 1981 to December 2008. Seventy-eight (78) cases were from the vulva and 84 from the vagina. Archival tissue blocks and or histopathological slides were missing for 10 of the cases and histologic classification could not be done. A total of 5913 gynecological cancers were seen within the study period. Vulvar cancers constituted 1.2% of all the gynecological cancers while vaginal cancers constituted 1.4%.

There were 4760 cancers of the cervix constituting 80.5% of the cases, 610 cancers of the ovary (10.3%), 381 cancers of the uterus (6.4%), 84 cancers of the vagina (1.4%) and 78 cancers of the vulva (1. 3%). Cancers of the vagina and the vulva are found to be the least common, being the 4th and the 5th most common.

The mean age of occurrence of vulvar and vaginal cancers was 49.7 years (± 18.5 years). The 95% confidence interval was 46.8 to 52.6 years. Peak incidence was in the 5th decade, age range was 1 to 99 years.

One hundred and fifty-two (152) cases were classified into various histologic types according to the WHO classifications of 2004 for vulvar and for vaginal tumors and the frequencies of the various types is as shown in **Table 1**.

The frequencies of vulvar and vaginal cancers within different time periods (viz. 1976-1995 by Babarinsa et al, the entire period of this study (1981-2008) and the periods in this study before and after the year 2000) are shown in **Table 2**.

A comparison of the mean of vulvar cancers seen before the year 2000 (1981-2000) with the mean after the year 2000 (2001-2008) using the *t* test was found to be statistically significant with a p value of $p = 0.00021$, a similar value for vaginal cancers was $p = 0.013$ and for the comparison of the means of the total numbers of vulvar and vaginal cancers before and after 2000 ($p < 0.0001$).

There was a 259% increase in the average number of vulvar cancers diagnosed per year from the period in this study before the year 2000 to the period afterwards while the average number of vaginal cancers per year decreased by 79%.

Table 1. The distribution of the various histological types of vulvar and vaginal cancers in this study.

HISTOLOGICAL TYPE	VULVA (% of the total no of vulvar cancers)	VAGINA (% of the total no of vaginal cancers)	TOTAL
Squamous Cell Carcinoma (SCC)	53 (73.61%)	49 (61.25%)	102 (67.11%)
SCC, NOS	41 (56.94%)	38 (47.50%)	79 (51.97%)
Keratinizing SCC	5 (6.94%)	3 (3.75%)	8 (5.26%)
Non-keratinizing SCC	2 (2.78%)	7 (8.75%)	9 (5.92%)
Verrucous carcinoma	2 (2.78%)	1 (1.25%)	3 (1.97%)
Microinvasive SCC	3 (4.17%)	*	3 (1.97%)
Adenocarcinoma	5 (6.94%)	15 (18.75%)	20 (13.16%)
Mucinous adenocarcinoma	1 (1.39%)	1 (1.25%)	2 (1.32%)
Clear cell adenocarcinoma	0	3 (3.75%)	3 (1.97%)
Adenocarcinoma, NOS	4 (5.56%)	11 (13.75%)	15 (9. 87%)
Small cell carcinoma	0	1(1.25%)	1 (0.66%)
Sarcomas	4 (5.56%)	7 (8.75%)	11 (7.24%)
Rhabdomyosarcoma	3 (4.17%)	7 (8.75%)	10 (6.58%)
Fibrosarcoma	1 (1.39%)	0	1 (0.66%)
Undifferentiated carcinoma	10 (13.9%)	7 (8.75%)	17 (11.18%)
TOTAL	72 (100%)	80 (100%)	152 (100%)

* The FIGO and the American Joint Committee on Cancer (AJCC) staging systems for vaginal tumors do not include superficially invasive (Stage 1A) SCC.

Table 2. A comparison of the incidence figures for vulvar and vaginal cancers for different time periods.

	Vulva Total (average number of cases /yr)	Vagina Total (average number of cases/yr)	Vulvar and vaginal malignancies Total (average number of cases /yr)
Babarinsa et al (1976-1995, 20 yrs)	30 (1.50)	46 (2.30)	76 (3.80)
This study (1981-2008, 28 yrs)	78 (2.78)	84 (3.00)	162 (5.79)
This study (1981-2000, 20 yrs)	32 (1.60)	49 (2.45)	81 (4.05)
This study (2001-2008, 8 yrs)	46 (5.75)	35 (4.38)	81 (10.13)

A comparison of the proportion of vulvar and vaginal cancers accounted for by vulvar cancers in the period before the year 2000 with the proportion accounted for by vulvar cancers after the year 2000 showed no statistically significant difference at $p < 0.05$. Similar *t* test analysis for the proportions of vaginal cancers before and after the year 2000 was also not statistically significant at $p<0.05$.

DISCUSSION

There were 5913 gynecological cancers seen over the 28-year period of this study. This may be compared with 2330 cancers seen over the 20-year period of the most recent previous study from the UCH, the study by Babarinsa et al.[1] These figures translate to an average of 211.2 and 116.5 gynecological cancers per year respectively and suggest an increase in the overall incidence of gynecological cancers.[1] In addition, a comparison of the means of vulvar and vaginal cancers before the year 2000 with the means of cancers from the same site after the year 2000 show statistically significant increases in the incidence of vulvar and vaginal cancers from the period of the first 20 years of this study to the last 8 years. The increase in the incidence of these cancers in our environment is likely due to increased health awareness among the population with the increasing use of hospital services.

An increase in the incidence of vulvar cancers in the United States, starting from the mid-1990s has been described by the National Cancer Institute (NCI) report for 2009.[10] There were no similar figures for vaginal cancers from the NCI; however reports from the United Kingdom [11] show that cancer of the vagina has remained stable over the past 25 years. It has been shown that the incidence of pre-invasive disease of the vulva has almost doubled over the past decade, and this may translate into a marked increase in the incidence of invasive vulvar carcinoma in the future.[12]

In our study, cancer of the cervix was the most common followed by cancers of the ovary, the uterus, the vagina and the vulva. In Nigeria, cancer of the cervix had previously been shown to be the most common gynecological cancer with cancers of the vulva and the vagina being the least common.[6] In the United States, cancer of the uterine corpus is the most common followed by cancer of the ovary, the cervix and then the vulva and the vagina.[13] In the United Kingdom, ovarian cancer is most common while vulvar and vaginal cancers are the least common.

The relative frequencies for cancers of the vulva and the vagina among gynecological cancers were found to be 1. 3% and 1.4% in this study. Corresponding figures from the study by Babarinsa et al [1] were 1.2% and 2% respectively. This suggests that even though the incidence of cancers of the vulva and vagina has increased, their relative frequencies among gynecological cancers have remained virtually stable with the incidence of the other gynecological cancers increasing at comparable rates.

In the United Kingdom, both cancers of the vulva and the vagina together account for 7% of gynecological cancers diagnosed in women.[8,11] In the United States, vulvar and vaginal cancers represent only 4-5% [3] and 2% [14] respectively of gynecological cancers. Worldwide rates for vulvar cancer range from less than 0.3 per 100,000 females in parts of Asia to about 1.6 per 100,000 females in North America and Europe. Rates for most parts of Africa fall about midway between the ones for Asia and North America.[8] This variation is probably related to differing prevalence of HPV infection in world regions, and other lifestyle factors, especially smoking, and their interaction with HPV.[8]

In this study overall, cancers of the vagina are more common than those of the vulva, this corroborates the findings in the studies by Babarinsa et al,[1] Kyari et al,[15] and Mohammed A et al [16] but opposes the findings from the study by Nwosu SO et al,[17] the United States of America[13] and the United Kingdom [8,11] When the cases diagnosed after the year 2000 were analyzed separately however, vulvar cancer had become more common.

When patients present late, as is often the case with these cancers in our environment, tumor is more likely to be seen involving multiple contiguous sites and this may lead to confusion in the determination of the primary site. The International Federation of Gynaecology and Obstetrics (FIGO) guidelines[18] state that patients with tumor involvement of the vagina along with the external cervical os proximally or the vulva distally should be classified as primary cervical or vulvar cancers respectively. Before a diagnosis of primary vaginal carcinoma can be established, a

5-10 year disease-free interval is required to rule out recurrent disease in those patients with a prior pre-invasive or invasive cervical or vulvar neoplasm. The FIGO guidelines [18] must be followed strictly in determining the primary site of origin. Failure to do this may result in an artificial switch whereby vaginal cancer may become more common than vulvar cancer even if this is not the true situation. It is known that while secondary tumors of the vulva are rare,[5] 80-90% of vaginal cancers are metastatic.[14]

The increased detection of vulvar cancers and the change in the relative distribution of vulvar and vaginal cancers seen after the year 2000, with vulvar cancers becoming more common than vaginal cancers, are likely due, at least in part, to the application of the FIGO guidelines in the determination of the primary site of origin of the gynecological cancers seen at the UCH. However, a comparison of the proportion of the total numbers of vulvar and vaginal cancers accounted for by vulvar or vaginal cancers in the period before the year 2000 with the proportion accounted for by cancers from the same primary site after the year 2000 showed no statistically significant difference at $p < 0.05$. This is probably due to the wide disparity observed in the percentage increase in the average number of vulvar cancers and the percentage decrease in the average number of vaginal cancers (259% versus 79%). A significant difference would have been most likely to be observed if the increase in the incidence of vulvar cancers had been associated with a comparable decrease in the incidence of vaginal cancers.

If the changes in the incidence of vulvar and vaginal cancers seen had been due to the use of the FIGO guidelines alone, each case of cervical or vulvar cancer accurately diagnosed by new criteria would have resulted in one less case of vaginal cancer, and a comparable decrease in the incidence of vaginal cancers. In this study, the changes resulting from the strict use of the FIGO guidelines have evidently been masked by a significant further increase in the incidence of vulvar cancers which contributes to a higher percentage increase than that from the use of the guidelines alone, and also an increase in the incidence of vaginal cancers contributing to a lower percentage decrease than is expected.

Making a distinction among vaginal, vulvar and cervical cancers is also of importance in that the primary site of gynecological cancer significantly impacts the choice of therapy. Standard primary treatment for vulvar cancer is surgery, with radiation usually being added to surgery in patients with stage III or IV disease.[19]

The proximity of the vagina to the bladder or rectum limits surgical treatment options for vaginal cancers and increases short- and long-term surgical complications and functional deficits involving these organs hence the choice of therapy is dependent on the following factors: the stage and the size of the lesion, proximity to radiosensitive organs or organs that preclude radical resection without unacceptable functional deficits (e.g., bladder, rectum, urethra), ability to retain a functional vagina, the presence or absence of the uterus, and whether there has been prior pelvic radiation therapy.[20]

Data from randomized trials are lacking for vaginal cancers and the choice of therapy is largely based on institutional experience with small case series.[20] For patients with carcinoma of the vagina in its early stages, radiation or surgery or a combination of these treatments are standard treatment.[20] Bulky tumors and late stage disease are often treated with chemotherapy by an extrapolation from treatment approaches used in cervical cancer, based on shared etiologic and risk factors. For cervical cancers, on the other hand, several randomized phase III trials have shown an overall survival advantage for cisplatin-based therapy given concurrently with radiation therapy for early stage and for advanced cancers.[21]

This study spans a period of 28 years including a significant part of the period when the relevant FIGO guidelines were not as widely used as they are today. The FIGO Staging Classifications and Clinical Practice Guidelines for Gynecological Cancers were published in 2000, and have been revised for the first time in March 2010. These 28 years also overlap with some years in the study by Babarinsa et al.[1] It is likely that some of the cases from the earlier years might have been diagnosed as vaginal cancer because the patient presented late with tumor involving multiple contiguous sites and the vagina was more significantly involved than the cervix or the vulva.

As mentioned earlier, the study by Babarinsa et al[1] showed that most of our patients present late and tend to default during treatment. Wu et al [2] studied vaginal cancers among different races in the United States and showed that black, Asian Pacific Island, and Hispanic women as well as older women were more likely to be diagnosed with late-stage disease, and these groups had lower 5-year relative survival rates than their white, non-Hispanic, and younger counterparts.

With early detection, vulvar cancer is highly curable. When lymph nodes are not involved, the five-year survival rate is slightly higher than 90 percent.[10] Even in developed nations, the management of vulvar carcinoma is hampered by the fact that diagnosis is delayed in most cases and by the choice of the proper surgical procedure.[12] The greatest difficulty in surgical management is with primary wound closure and healing, and wound breakdown and sepsis occur commonly.[22]

The mean age in this study was 49.7 years with peak occurrence in the 5th decade. Other previous studies from Nigeria show that most patients with vulvar and vaginal cancers are older than 50 years.[1,15,16,17] In the United States of America, both cancers are also most commonly seen in persons older than 50 years.[2,3]

SCC constitutes 73.61% of vulvar cancers and 61.25% of vaginal cancers seen in this study. Squamous cell carcinoma has previously been reported to be the most common malignant tumor of the vulva and vagina by a previous study from Nigeria [1] and several reports from the developed nations [3,8,11] sometimes constituting as many as 95% of the cases

seen. Other less common carcinomas seen include basal cell carcinoma and adenocarcinoma. Non-epithelial malignant tumors of the vulva include sarcomas, melanomas, Merkel cell carcinoma, yolk sac tumor, lymphomas and leukaemias. In the vagina, the most important non-epithelial tumors are malignant melanoma and sarcoma botryoides.[4]

Apart from keratinizing and non-keratinizing SCC, two other specific subtypes of SCC are seen in this study: verrucous carcinoma and superficially invasive SCC. Three (3) cases of verrucous carcinoma were found in this study. Two of the cases were found in the vulva in patients aged 45 and 74 years. The one case found in the vagina was in a 70 year old patient. Verrucous carcinoma (VC) of the vulva is a rare variant of squamous cell carcinoma (SCC) of the vulva that afflicts older women, usually older than 70 years, and is characterized by a well-differentiated morphology with minimal nuclear atypia.[23] Three cases of superficially invasive SCC (SISCC, previously known as microinvasive carcinoma) were found in the vulva constituting 4.17% of all the vulvar cancers seen in this study. Superficially invasive SCC is FIGO Stage 1A carcinoma; it is defined as a single lesion measuring 2 cm or less in diameter and with a depth of invasion of 1 mm or less. SISCC has been shown to have a minimal risk of lymph node metastasis and it is associated with excellent prognosis.[24]

In this study, 5 cases of adenocarcinoma were seen in the vulva, constituting 6.94% of vulvar cancers and 15 cases in the vagina constituting 18.75% of the vaginal cancers seen in this study. The specific subtypes seen in this study include mucinous and clear cell adenocarcinomas. Adenocarcinomas of the vulva may arise in the Bartholin's glands, endometriosis or ectopic cloacal tissue.[5]

Clear cell adenocarcinomas of the vagina (and the cervix) are associated with in utero exposure to diethylstilbestrol (DES). The peak incidence of DES- associated adenocarcinoma of the vagina is at young ages (less than 30 years) while adenocarcinomas that are not associated with DES exposure occur primarily during postmenopausal years.[5]

The association between the clear cell carcinomas and in utero exposure to DES was first reported in 1971. The incidence of this disease, which is highest for those exposed during the first trimester, peaked in the mid-1970s, reflecting the use of DES in the 1950s.[20] It is now extremely rare.[20] Non–DES-associated adenocarcinomas generally have a worse prognosis than SCC tumors, but DES-associated clear cell tumors have a relatively good prognosis.[20]

In this study, one case of small cell carcinoma is found in the vagina, constituting 1.25% of vaginal cancers. Small cell carcinoma is a carcinoma of neuroendocrine differentiation.[4] In the vulva, it tends to occur in the Bartholin's gland.[5]

Ten (10) cases (13.9%) of undifferentiated carcinoma are seen in the vulva in this study and 7 cases (8.75%) in the vagina. This is a carcinoma lacking evidence of glandular, squamous, neuroendocrine or other types of differentiation.[4,5]

Four (4, 5.56%) sarcomas are seen in the vulva and 7 (8.75%) in the vagina. Worldwide, primary sarcomas of the vulva constitute between 1 and 2% of all vulvar and vaginal malignancies.[4,5] In this study, embryonal rhabdomyosarcoma (sarcoma botyroides) is the most common sarcoma seen in both the vulva and the vagina; all but one of all the cases of vulvar and vaginal cancers found in persons younger than 10 years of age were diagnosed as such. Embryonal rhabdomyosarcoma is a malignant neoplasm exhibiting striated muscle differentiation that occurs almost exclusively in children younger than 10 years of age.

Even though the specific etiology of most vulvar epithelial tumors is unknown, Human papillomavirus and cigarette smoking are known to be risk factors.[5]

In 2002, Olayemi et al reported a case of vulvar carcinoma in pregnancy from this hospital [25] which showed tumor arising in condyloma acuminata, and corroborates the important role played by HPV in vulvar cancer disease.

Vulvar SCC has been shown to be a multifactorial disease following two separate and independent pathways, an HPV-dependent pathway with classic VIN as precursor lesions and an HPV-independent pathway associated with differentiated VIN and/or lichen sclerosus.[26] HPV-positive carcinomas account for one-quarter to one-third of cases, occur in women on average 20 years younger than in HPV-negative, and are associated with multiple lower genital tract neoplasia.[27]

Classic VIN is predominantly of the warty and basaloid types and these types of squamous intraepithelial lesions, along with the corresponding carcinoma types are associated with HPV infections, most predominantly HPV 16.[4,5] Verrucous carcinoma is also associated with HPV, usually of type 6 or 11.[4,5]

Persistent infection with high risk HPV infection is a major risk factor for both vaginal intraepithelial neoplasia (VAIN) and SCC.[4] The fact that VAIN and vaginal SCC are much less common than cervical neoplasia has been explained by the absence of a vulnerable transformation zone in the vagina.[4]

CONCLUSION

We conclude that strict adherence to the FIGO guidelines is crucial in determining the primary site of gynecological cancers in patients with advanced local disease.

With per capita total expenditure on health of US$8 per year in Nigeria [5] and a retail price of up to $125 per dose or $375 for the full series consisting of 3 doses [28] it appears that HPV vaccines may be out of the reach of the average Nigerian and without government funding, it may not be the ultimate solution for reducing the burden of disease from anogenital cancers and other HPV-associated diseases at this time.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to declare.

REFERENCES

1. Babarinsa IA, Fakokunde FA, Ogunbiyi JO, Adewole IF. Vulvar and vaginal cancers as seen at the University College Hospital, Ibadan, Nigeria. Afr J Med Med Sci. 1999;28(1-2):77-80.
2. Wu X, Matanoski G, Chen VW, et al. Descriptive epidemiology of vaginal cancer incidence and survival by race, ethnicity, and age in the United States. Cancer Supplement. 2008;113(S10):2873-2882.
3. Saraiya M, Watson M, Wu X, et al. Incidence of in situ and invasive vulvar cancer in the US 1998-2003. Cancer Supplement. 2008;113(S10):2865-2872.
4. Andersen ES, Paavonen J, Murnaghan M, et al. In: Tavassoli FA, Devilee P, Editors. WHO Classification of Tumors No 4. Pathology and Genetics Tumors of the Breast and Female Genital Organs. Lyon, France, 2003, 291-311.
5. Wilkinson EJ, Teixera MR, Kempson RL, Hendrickson MR. Vulva. In: Tavassoli FA, Devilee P, Editors. WHO Classification of Tumors No 4. Pathology and Genetics Tumors of the Breast and Female Genital Organs. Lyon, France, 2003, 313.
6. Nigeria: Human Papillomavirus and Related Cancers, Summary Report Update 2009, WHO/ICO HPV Information Centre, © World Health Organization and Institut Catala d'Oncologia 2010. http://apps.who.int/hpvcentre/statistics/dynamic/ico/country_pdf/NGA.pdf . Accessed on 4/1/2013.
7. Cancer Facts and Figures for 2009, © American Cancer Society, 2009, available at http://www.cancer.org/downloads/STT/500809web.pdf.
8. UK vulval cancer incidence statistics. Cancer research UK- New & resources - Cancer Stats - 26 types of cancer - Vulval cancer – Incidence. http://info.cancerresearchuk.org/cancerstats/types/vulva/incidence/index.html. Accessed on 4/1/2013.
9. Thomas JO, Herrero R, Omigbodun AA, et al. Prevalence of papillomavirus infection in women in Ibadan, Nigeria: a population-based study. Br J Cancer. 2004;90(3):638-645.
10. SEER Stat Fact Sheets - Cancer of the vulva, © National Cancer Institute 2010, United States. http://seer.cancer.gov/statfacts/html/vulva.html. Accessed on 4/1/2013.
11. UK vaginal cancer incidence statistics. Cancer research UK- New & resources - Cancer Stats - 26 types of cancer - Vaginal cancer - Incidence, http://info.cancerresearchuk.org/cancerstats/types/vagina/incidence/index.html. Accessed on 4/1/2013.
12. Higgins RV, Naumann RW, Hall J. eMedicine Specialties > Obstetrics and Gynecology > Gynecologic Surgery, Surgical Treatment of Vulvar Cancer available at http://emedicine.medscape.com/article/268880-overview.
13. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin. 2009;59(4):225-249.
14. Serur E. Vaginal cancer. www2.saintfranciscare.com/serur vaginalcancer. Accessed on 4/1/2013.
15. Kyari O, Nggada H, Mairiga A. Malignant tumours of female genital tract in North Eastern Nigeria. E Afr Med J. 2004;81(3):142-145.
16. Mohammed A, Ahmed SA, Oluwole OP, Avidime S. Malignant tumours of the female genital tract in Zaria, Nigeria: Analysis of 513 cases. Ann Afr Med. 2006;5(2):93-96.
17. Nwosu SO, Anya SE. Malignancies of the female genital tract at the university of Port Harcourt teaching hospital: a ten year review - 1990-1999. Niger Postgrad Med J. 2004;11(2):107-109.
18. Benedet JL, Bender H, Jones H III, Ngan HY, Pecorelli S. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. Int J Gynaecol Obstet. 2000;70(2):209-262.
19. Vulvar cancer treatment (PDQ®)- Health professional version. © National Cancer Institute, at the National Institutes of Health. http://www.cancer.gov/cancertopics/pdq/treatment/vulvar/HealthProfessional. Accessed on 4/1/2013.
20. Vaginal cancer treatment (PDQ®)- Health professional version. © National Cancer Institute, at the National Institutes of Health. http://www.cancer.gov/cancertopics/pdq/treatment/vaginal/HealthProfessional. Accessed on 4/1/2013.
21. Cervical cancer treatment (PDQ)- Health professional version. National Cancer Institute, at the National Institutes of Health. http://www.cancer.gov/cancertopics/pdq/treatment/cervical/HealthProfessional. Accessed on 4/1/2013.
22. Gharoro EP, Okonkwo CA, Onafowokan O. Adenocarcinoma of the Bartholin's gland in a 34 year old multipara. Acta Obstet Gynaecol Scand. 2001;80(3):279-280.
23. Nascimento AF, Granter SR, Cviko A, Yuan L, Hecht JL, Crum CP. Vulvar Acanthosis With Altered Differentiation: A Precursor to Verrucous Carcinoma? Am J Surg Pathol. 2004;28(5):638-643.
24. Yoder BJ, Rufforny I, Massoll NA, Wilkinson EJ. Stage IA Vulvar Squamous Cell Carcinoma: An Analysis of Tumor Invasive Characteristics and Risk. Am J Surg Pathol. 2008;32(5):765-772.
25. Olayemi O, Aimakhu CO, Omigbodun AO, et al. Vulval carcinoma in pregnancy. Obstetric case reports. J Obstet Gynaecol. 2002;22(4):441-442.
26. Skapa P, Zamecnik J, Hamsikova E, et al. Human Papillomavirus (HPV) Profiles of Vulvar Lesions: Possible Implications for the Classification of Vulvar Squamous Cell Carcinoma Precursors and for the Efficacy of Prophylactic HPV Vaccination. Am J Surg Pathol. 2007;31(12):1834-1843.
27. Scurry JP, Vanin K. Vulvar squamous cell carcinoma and lichen sclerosus. Australas J Dermatol. 1997;38(Suppl 1):S20-534
28. Fact Sheet on HPV vaccines, Centers for Disease Control and Prevention, Department of Health and Human Services, Sexually Transmitted Diseases > Health Communication > Fact Sheets > HPV Vaccine Information For Young Women, available at http://www.cdc.gov/std/hpv/STDFact-HPV-vaccine-young-women.htm#hpvvac1.