Research Article

Histopathological Patterns of Cervical Cancer Among Females Presenting to Makerere University Pathology Core Reference Laboratory. A 5-Year Review

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Background and Aim: The global burden of cervical cancer is heavy in low- and middle-income countries, having highest rates in sub-Saharan Africa. Cervical cancer is the leading cause of cancer morbidity and mortality in Ugandan women with estimated 6959 new cases and 4607 deaths in 2020. The histopathological differentiation of cervical cancer is a major determinant in treatment options and prognosis of disease. However, there is paucity of data regarding this in Uganda. The study aimed to determine the histopathological pattern of cervical cancer among females presenting to Makerere university pathology core reference laboratory.

Methods: A retrospective cross-sectional study employing the use of quantitative methods of data collection was conducted within Makerere university pathology core reference laboratory. Information on patients with cervical cancer diagnosis by histology from 2017-2021 was obtained and analyzed using SPSS version 18.

Results: A total of 120 patients from 2017-2021 were recruited. The mean age was 47.5(SD 13.1), the youngest and oldest patients were 21 and 80 years respectively. Cervical cancer was more prevalent in women aged between 35 to 54 years 77(64.2%) and women with HIV 26(21.7%). Squamous cell carcinoma presents in 102(85%) patients was the most prevalent pattern of cervical cancer. This was followed by adenocarcinoma 7(5.8%) and adenosquamous 5(4.2%).

Conclusions: Cervical cancer is predominant among women with HIV and women aged 35-55 years. Squamous cell carcinoma is the most prevalent pattern of cervical cancer in Uganda present in every 9 out 10 patients. Routine screening of all HIV positive women and women aged 35 and above is recommended

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List of Abbreviations

- AC……Adenocarcinoma
- CIN……Cervical Intraepithelial Neoplasia
- ECC……Endocervical curettage
- HIV……Human Immunodeficiency Virus
- HMIS……Health Management Information System
- HPV……Human Papilloma Virus
- LMICs……Low- and middle-income countries
- SCC……Squamous Cell Carcinoma
- SEER……Surveillance, Epidemiology, and End Results
- VIA……Visual Inspection with Acetic acid
- VII……Visual Inspection with Lugol's Iodine
- WHO……World Health organization

List of Operation Definitions

- **Cervical cancer;** Cervical cancer is a type of cancer that occurs in the cells of the cervix — the lower part of the uterus that connects to the vagina.
- **Pattern;** any regularly repeated arrangement of something.
- **Histopathology;** Refers to the microscopic examination of tissue in order to study the manifestations and characteristics of a disease.
- **Histopathological pattern;** Characteristic of particular tumors or group of tumors as seen under the microscope.

Keywords: histopathological patterns, cervical cancer, Uganda.

CHAPTER INTRODUCTION

1.0 Introduction

Cervical cancer is a type of cancer that begins on the mouth of the uterus (cervix). Cells on the cervix begin to grow slowly and abnormally over several years. These early (pre-cancerous) changes can disappear on their own without causing problems, however in some women, they grow into cancer if they are not identified and treated early [1].

The common cause of cervical cancer is Human Papilloma Virus (HPV). HPV is responsible for 99.7% of cervical cancer and Infects 75 - 80% of sexually active adults at some point, however, it can be cleared by the body's immune system most of the time and is preventable. Over 100 types of HPV are currently known, most are not associated with cervical cancer or genital warts. The High risk types (16, 18) are associated with cancer and the low risk types (6, 11) are associated with genital warts [2].

There are different histological patterns of cervical cancer ranging from premalignant lesions (cervical intraepithelial neoplasia), squamous cell carcinoma, adenocarcinoma and others. Histological screening and diagnosis of cervical cancer is very crucial in prevention, early detection and treatment of cervical cancer and is recommended in all women of reproductive age [2].

The aim of this study was to assess the patterns of cervical cancer among females presenting to Makerere university pathology core reference laboratory by conducting a five-year review.

1.1. Problem statements

The global burden of cervical cancer is heavily concentrated in low- and middle-income countries (LMICs), having the highest rates in sub-Saharan Africa (SSA) [3]. In Uganda, due to an increased burden of HIV, the prevalence, morbidity and mortality from cervical cancer has been increasing in the recent years. Uganda ranks seventh in the world for cervical cancer incidence, with an estimated rate of 56.2 per 100 000 people in 2020 (compared to a global rate of 13.3) [4]. Cervical cancer is the leading cause of cancer morbidity and mortality in Ugandan women with an estimated 6959 new cases and 4607 deaths in 2020 [4].

The histopathological differentiation of cervical cancer is a major determinant in treatment options for cervical cancer and is a major determinant of prognosis of the disease. For example a study done in Romania demonstrated that cervical cancer patients with adenocarcinomas and adeno-squamous

carcinomas had a significantly poorer treatment response to chemo-radiotherapy than those with squamous cell carcinomas [5]. There is paucity of data regarding the histopathological cervical cancer patterns in Uganda. This makes it difficult to plan for appropriate treatment modalities aimed at maximizing treatment benefits for cervical cancer patients.

1.2. Significance of the study

The information generated from this study will inform the country (Uganda) on the histopathological patterns of cervical cancer in Uganda. This will help in proper planning of appropriate treatment and management of cervical cancer. The information will help oncologists and policy makers to appropriate health guidelines for cervical cancer basing on disease prevalence rates for different histopathological patterns of cervical cancer. Furthermore, the information will act as a guide for further research on cervical cancer in Uganda.

1.3. Justification

Histopathology and cytopathology form the scientific and clinical basis for current prevention and treatment of cervical cancer. Histopathology determines treatment of cancer and precancer through classifying into a diagnosis the patterns of microscopic organization of cells in tissue sections from biopsy or surgical specimens. Understanding the histopathological patters of cervical cancer in Uganda will provide a basis for designing interventions to reduce cervical cancer morbidity and mortality. This will help reduce cancer related deaths and will lead to socioeconomic transformation.

1.4. Research questions

What are the histopathological patterns of cervical cancer in Uganda?

1.5. Objectives

General objective

To determine the pattern of cervical cancer among females presenting to Makerere university pathology core reference laboratory.

Specific objectives

To determine the histopathological pattern of cervical cancer among females presenting to Makerere university pathology core reference laboratory.

1.6. Scope of the study

Content scope

The study was limited to assessing only the histopathological pattern of cervical cancer among females presenting to Makerere university pathology core reference laboratory.

Geographical scope

The study was conducted with in Makerere university pathology core reference laboratory found at Makerere University College of Health Sciences in Mulago hill, Kampala Uganda.

Time scope

The study took a total period of 3 months from September 2022 to November 2022. The researcher reviewed the laboratory documents from 2021 to 2017 to assess the histopathological pattern of cervical cancer among females presenting to Makerere university pathology core reference laboratory.

CHAPTER TWO: LITERATURE REVIEW

2.0. Background

Worldwide, cervical cancer is the fourth most frequent cancer in women with an estimated 604 000 new cases in 2020 [2]. Of the estimated 342,000 deaths from cervical cancer in 2020, about 90% of these occur in low- and middle-income countries. Women living with HIV are 6 times more likely to develop cervical cancer compared to women without HIV, and an estimated 5% of all cervical cancer cases are attributable to HIV [6].

In Uganda, the crude incidence rate of cervical cancer is estimated at 30 per 100 000, while the mortality rate was estimated at 19.9 per 100 000 [7]. Cervical cancer is the number one cause among

women of both age-standardized cancer-related incidence and cancer-related deaths from all cancers in Uganda [7].

Like in other parts of the world, the involvement of human papilloma virus (HPV) infection in this malignancy in Uganda is comparable to the rest of the world with HPV-16 and HPV-18 as the major oncogenic strains [8]. A 2011 review reported a number of estimates of high-risk HPV prevalence from 20 studies, ranging from 10.2% to 40% among HIV negative women and ranging from 37% to 100% among HIV positive women. The HPV prevalence estimates among women with normal cytology included in the HPV Information Centre report range from as low as 15.2% in women aged 25-60 to as high as 73.2% in women aged 12-24 [9]. Most of the prevalence studies were conducted prior to the introduction of the HPV vaccination programs in Uganda; therefore, these estimates may not reflect the current situation.

The WHO recommends a screen-and-treat strategy to reduce incidence of cervical cancer [2]. The target age group is women 25 to 49 years old. Screening occurs every 3 years for HIV-negative women and annually for HIV-positive women. Midwives and nurses are the primary providers of cervical cancer screening as well as treatment [10]. The screening methods include visual inspection with acetic acid (VIA), visual inspection with Lugol's iodine (VII), colposcopy, HPV testing and pap smear. Patient who screen positive should have a histological diagnosis before they are confirmed of cervical cancer [1].

Prior to enrollment of patients for cervical cancer treatment, a diagnostic or confirmatory test must be done to make a definitive diagnosis or confirmation of pre-cancer or cancer lesions [9]. Colposcopy, biopsy and endocervical curettage (ECC) are the most commonly used diagnostic tests for cervical cancer. Colposcopy and endocervical curettage are not routinely done in Uganda, and thus biopsy is the gold standard for the diagnosis of cervical cancer in Uganda. Biopsy is used to determine the degree of abnormality of the cell changes at the cervix and to rule out cancer. After examination, the result is classified as normal, as cervical intraepithelial neoplasia (CIN), or as invasive carcinoma. The precancerous lesions are classified as low-grade (CIN1) or high-grade (CIN2 and CIN3, collectively referred to as CIN2+) pre-cancer. The classification is based on the thickness of the abnormal epithelium: the deeper the abnormal cells reach from the basement membrane toward the upper layer of cells, the higher the degree. For cancerous lesions, the histological pattern of the malignancy is also determined [1].

There are many histopathological patterns of cancer of the cervix. This must be determined as it influences treatment and prognosis of the disease. The common histopathological patterns are Squamous cell carcinoma (SCC), adenocarcinoma, adenoid cystic carcinoma, adeno-squamous carcinoma, clear cell carcinoma and mucinous carcinoma. Some of the tumors can be well differentiated, moderately differentiated or poorly differentiated tumors [11]. The aim of this study is to assess the histopathological patterns of cervical cancer in Uganda.

2.1. Histopathological patterns of cervical cancer

According to Dutta's Textbook of Gynecology, the commonest histological type of cervical cancer is squamous cell carcinoma (85-90%) either well-differentiated or moderately or poorly differentiated. The sources of the squamous epithelium which turn into malignancy arise from squamo-columnar junction or squamous metaplasia of the columnar epithelium. Squamous cell carcinoma is further subdivided histologically into three groups: (i) large cell keratinizing, (ii) large cell non-keratinising and (iii) small cell type. Patients with small cell type have got poor prognosis compared to the large cell types. There's also a rare type; basaloid squamous cell carcinoma (BSCC)which is an aggressive variant of oral squamous cell carcinoma. Some patients present with adenocarcinomas, and others less commonly with mixed carcinomas (features of both squamous cell carcinoma and adenocarcinoma) of the cervix [12].

Other histopathological patterns of cervical cancer are adenocarcinoma (10–15%) which develops from the endocervical canal, either from the lining epithelium or from the glands. Currently increased number of cervical adenocarcinomas are observed specially in the younger
age group. The majority (80%) of them are purely endocervical type. The remainders are endometrioid, clear cell, adenosquamous or a mixed type. Adenoma-malignum is an extremely well-differentiated adenocarcinoma with favorable prognosis. Neuroendocrine tumors, sarcomas and lymphomas are rare tumors of the cervix [12][13].

In a review conducted in Nigeria, poorly differentiated squamous cell carcinoma was the leading variants of cervical cancer. Squamous cell carcinoma (SCC) was seen in 90.8% patients while 7.1% patients had adenocarcinoma. One patient each had adenoid cystic carcinoma, adenosquamous carcinoma, clear cell carcinoma and mucinous carcinoma [11]. In the same study, majority of the patients, (50.5%) had poorly differentiated tumors, 32.7% had well differentiated tumors, while the rest 16.8% had moderately differentiated tumors [11].

In another review conducted in India, the most common malignancy was squamous cell carcinoma (88.1 %) among which moderately differentiated squamous cell carcinoma comprised (73.1 %) followed by well differentiated squamous cell carcinoma (11.3 %) and poorly differentiated (3.7 %). Other variants of cervical cancer were papillary, adenosquamous and basaloid variants [14].

In a study done in Kenya in East Africa, the most prevalent histological type of cervical cancer was squamous cell carcinoma (SCC) (89.9%), followed by adenocarcinoma (AC) (5.6%). Two patients had anaplastic carcinoma, and another two had sarcoma of the cervix. Among those with SCC, most had moderately differentiated SCC (39.2%), with 32.0% and 21.3% having poorly differentiated and well differentiated disease respectively. At the time of diagnosis, the majority of patients (80.5%) presented with stage 2B disease or above [15].

Since histopathology is a cornerstone in the detection and the diagnosis of cervical cancer, studies have studied how histopathological classification of cervical cancer influence the management, treatment and surveillance planning of newly diagnosed cervical cancer. A study conducted in united states using the United States Surveillance, Epidemiology, and End Results (SEER) population data found out that Small cell carcinoma and adenocarcinomas were generally associated with poorer survival [16]. In the same study, cause-specific mortality hazard ratios by histological type relatively to non-micro-invasive squamous cell carcinoma were: micro invasive squamous cell carcinoma 0.28, carcinoma not otherwise specified 0.91, non-mucinous adenocarcinoma 1.06, adenosquamous carcinoma 1.35, mucinous adenocarcinoma 1.52 and small cell carcinoma 1.94. This study therefore greatly highlights the importance of histopathological classification of cervical cancer in determining treatment choices, morbidity and mortality due to the disease [16].

Despite known histopathological patterns of cervical cancer in different countries, the case is different for Uganda. There is a knowledge gap regarding histopathological patterns of cervical cancer among cervical cancer patients in Uganda. The purpose of this study was to address the gap.

CHAPTER THREE: RESEARCH METHODS

3.1. Study design

This was a quantitative retrospective cross-sectional study. This study design helped the researcher collect enough information due for a period of 5 years in a short period of time.

3.2. Study area

The study was conducted within Makerere university pathology core reference laboratory found at Makerere University College of Health Sciences in Mulago hill, Kampala Uganda. The Makerere University pathology laboratory is a core reference laboratory in Uganda receiving different types of specimens from all over the country. Therefore, the information generated on cervical cancer patterns could be representative of the whole of Uganda.

3.3. Study population

The study population were cases of cervical cancer that had histology done from Makerere university pathology core reference laboratory from 2017 to 2021 as documented in the laboratory Health Management Information System (HMIS) books and computers.

3.4. Selection criteria

This includes both inclusion and exclusion criteria

Inclusion criteria

- Patients with a positive cervical cancer histology done from Makerere university pathology core reference laboratory.
- Patient information must have been recorded in the HMIS books or in the computer
- The histological diagnosis must have been made from 2017 to 2021

3.5. Sample size determination

Exclusion criteria

Patient information incomplete such as unspecified type of cervical cancer. A total of 5 studies were excluded from the study due to missing information. This was mainly due to poor handwriting of the technician as the written information could not be read by the researcher during data collection.

Total population sampling was used and therefore all reports belonging to patient's that met the inclusion /exclusion criteria were recruited in the study.

3.6. Sampling technique

Total population were be captured and processed for data analysis.

3.7. Data collection methods

The data collection guide was developed and then exported to a mobile data collection platform. For the purpose was therefore transferred from laboratory HMIS books and computers to Epicollect 5.

3.8. Data analysis

The Data collected was analyzed using SPSS version 18.

3.9. Quality control

Pre-testing data collection tool was done before starting data collection to ensure that the tool is able to capture all necessary information.

Only complete information was entered into the mobile data collection tool.

3.10. Ethical considerations

Ethical approval was obtained from the School of Biomedical Sciences Institution Review Board.

Administrative clearance was obtained from Makerere university pathology core reference laboratory.

Privacy and confidentiality of patient information was mentioned all the times by concealing patient identifiers and using strong passwords in computers containing patient data.

3.11. Dissemination of results

A dissertation has been written and shared with Sir Albert Cook library at Makerere University College of Health Sciences, Uganda cancer institute and Uganda Ministry of Health

A peer-review publication will be written.

Presentation of findings at both national and international conferences will be made.

3.12. Study limitations

The accuracy of the information depended on the expertise of the pathologist who reported it. This raises a question of reliability of the findings. The study was a single-laboratory-based review and as

such inadequate to draw conclusions, but it does shed some light on pathological pattern of cervical cancer in Uganda.

CHAPTER FOUR: RESULTS

Sociodemographic characteristics of the respondents

A total of 120 patients from 2017 to 2021 were recruited into the study. The mean age of the patients was 47.5 (Standard deviation 13.1), the youngest patient was 21 years and the oldest was 80 years of age. Cervical cancer was more prevalent in women aged between 35 to 54 years 77(64.2%) and women from central Uganda 59 (49.2%). Kampala 24 (20.0%), Wakiso 16 (13.3%) and Rukungiri 12 (10.0%) districts were the most affected districts. The sociodemographic characteristics of the respondents are shown in the table below.

Variable	Frequency	Percentage
Age		
Less than 35	21	17.5
35 -44	34	28.3
45-54	33	27.5
55-64	21	17.5
65-80	11	9.2
Address		
Central Uganda	59	49.2
Western Uganda	29	24.2
Eastern Uganda	24	20.0
Northern Uganda	8	6.7
Tribe		
Muganda	49	40.8
Munyankole	15	12.5
Musoga	9	7.5
Munyoro/Mutoro	6	5.0
Others	41	34.2

Table 1. Sociodemographic characteristics of the respondents

Presenting complaints and associated medical conditions

Majority of cervical cancer patients had associated HIV infection 26(21.7%) and presented with complaints of vaginal bleeding (49.8%) and vaginal discharge 12(10.0%). The stage of the cervical cancer at the time of diagnosis for majority of the patients 55 (45.8%) could not be determined.

However, 24 (20.0%) patients had cervical cancer localized, 32 (26.7%) had a local spread and 3 (2.5%) patients had distant metastases.

Variable	Frequency	Percentage
Associated condition		
HIV/AIDS	26	21.7
Pregnancy	4	3.3
Confirmed HPV infection	11	9.2
Family history of cervical cancer	3	2.5
None of the above	53	44.2
Presenting complaints		
PV bleeding	49	40.8
PV discharge	12	10.0
Others	59	49.2
Stage at diagnosis		
Localized	24	20.0
Local spread	32	26.7
Regional spread	4	3.3
Distant metastases	3	2.5
Stage not determined	55	45.8

Table 2. Frequency of presenting complaints, associated conditions

Histopathological patterns of cervical cancer

Squamous cell carcinoma presents in 102 (85%) patients was the most prevalent pattern of cervical cancer. This was followed by adenocarcinoma 7 (5.8%) and adenosquamous 5 (4.2%) histological patterns of cervical cancer.

The squamous cell carcinoma in majority of the respondents was large cell keratinizing and moderately differentiated.

Variable	Frequency	Percentage
Subdivisions of SSC		
Large cell keratinizing	57	55.9
Large cell non-keratinising	39	38.2
Small cell type.	6	5.9
Differentiation status		
Well-differentiated	17	16.7
Moderately	62	60.8
Poorly differentiated.	24	23.5

Table 3. Patterns of squamous cell carcinoma

CHAPTER FIVE: DISCUSSION OF FINDINGS

Since histopathology is a cornerstone in the detection and the diagnosis of cervical cancer, studies have studied how histopathological classification of cervical cancer influence the management, treatment and surveillance planning of newly diagnosed cervical cancer. There has been a knowledge gap regarding histopathological patterns of cervical cancer among cervical cancer patients in Uganda. The purpose of this study among patients examined at Makerere university pathology core reference laboratory.

This study showed that cervical cancer was more prevalent in women aged between 35 to 54 years with an average age of diagnosis at 47.5 years. The findings are consistent with a 2022 report from United States of America which reported that cervical cancer is most frequently diagnosed in women between the ages of 35 and 44 with the average age at diagnosis being 50 [17]. The prevalence of cervical cancer increases with age due to long-lasting infection with certain types of human papillomavirus (HPV)

among women, which later causes cervical cancer due to diminished immune functioning associated with increase in age.

The present study demonstrate that majority of cervical cancer patients had associated HIV infection. The findings are consistent with a report from WHO which showed that women living with HIV are 6 times more likely to develop cervical cancer compared to women without HIV [18]. In fact, HIV is responsible for around 5% of all cervical cancer cases worldwide and is the leading cause of death among women living with HIV [19]. Although the mechanism by which HIV increases risk of cervical cancer is not completely understood, studies suggest that HIV-induced immunosuppression leads to an inability to control the expression of HPV and the production of HPV oncoproteins E6 and E7 [20][21]. According to Hawes and colleagues, this risk appears to be associated with increased HPV persistence that may result from immunosuppression related to HIV [22].

In the present study, squamous cell carcinoma patients was the most prevalent pattern of cervical cancer (85%). This was followed by adenocarcinoma 5.8% and adenosquamous 4.2% histological patterns of cervical cancer. The findings of this study correspond to findings of a study done by [23] which reported that was accounting for three-fourths of all cervical cancers. In the same study, adenocarcinoma and adenosquamous cell carcinoma represent 10–15%, and other or unspecified histology represent the remaining 10–15% [23]. However, a study done by [16] reported an overall increasing number of adenocarcinomas and adenosquamous carcinomas. A predorminace of SCC in Uganda imply that treatment of cervical cancer with chemotherapy would increases the changes of response to treatment and decline in mortality. This is because SCC is associated with high chances of survival than other histological such as small cell carcinoma, several subtypes of adenocarcinoma- mucinous, clear cell, and common type of adenocarcinoma- and denosquamous carcinoma [16].

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

Conclusions

1. Cervical cancer is more prevalent among women suffering from HIV and older women aged between 35 to 54 years.
2. Squamous cell carcinoma is the most prevalent pattern of cervical cancer in Uganda present in every 9 out 10 cervical cancer patients.

3. Moderately differentiated and large cell squamous cell carcinoma are the predominant patterns of squamous cell carcinoma in Uganda.

Recommendations

1. Routine screening of all HIV positive women and women aged 35 years and above is recommended.
2. Identified patients of cervical cancer should be treated immediately as they are likely to have cervical cancer pattern with a high prognostic value.

Declarations

Ethics approval and consent to participate

The study received all required ethical approval and privacy and confidentiality was observed.

Consent for publication

Not applicable.

Availability of data and materials

All information fronted in this article can be retrieved from the Makerere University Pathology laboratory.

Competing interests

The authors declare no competing interests

Author's contributions

- MM conceptualized the context and methodology of the study and was the major contributor and editor of the manuscript.
- LF did the data collection from the laboratory, analysis and interpretation.
- Both authors read and approved the final manuscript.

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References

1. ^a, ^b, ^c*Uganda_Cancer_Institute. (2017). Cevical Cancer Information, Education and Communication Bo oklet for Health Workers.*
2. ^a, ^b, ^c, ^d*WHO. (2022). Cervical cancer.*
3. ^*Kirsten Beyer, Simon Kasasa, Ronald Anguzu, Robert Lukande, Sarah Nambooze et al. (2022). High-r esolution disease maps for cancer control in low-resource settings: A spatial analysis of cervical cancer i ncidence in Kampala, Uganda. Journal of Global Health. 12.*
4. ^a, ^b*Uganda_Fact_Sheet. (2020). Uganda Fact Sheet. 2020. Available: https://gco.iarc.fr/today/data/fact sheets/populations/800-uganda-fact-sheets.pdf. Accessed: 11 April 2021.*
5. ^*Silviu Voinea, Cătălin Gabriel Herghelegiu, Angela Sandru, Raluca Gabriela Ioan, Roxana Elena Bohilț ea et al. (2021). Impact of histological subtype on the response to chemoradiation in locally advanced ce rvical cancer and the possible role of surgery. Experimental and therapeutic medicine. 21(1):1-1.*
6. ^*Dominik Stelzle, Luana F Tanaka, Kuan Ken Lee, Ahmadaye Ibrahim Khalil, Iacopo Baussano et al. (2 021). Estimates of the global burden of cervical cancer associated with HIV. The Lancet Global Health. 9 (2):e161-e169.*
7. ^a, ^b*Carolyn Nakisige, Jessica Trawin, Sheona Mitchell-Foster, Beth A Payne, Angeli Rawat et al. (2020). Integrated cervical cancer screening in Mayuge District Uganda (ASPIRE Mayuge): a pragmatic sequenti al cluster randomized trial protocol. BMC public health. 20(1):1-13.*
8. ^*Hala Mohammed Yousif, Abdulkader Mohammed Albasri, Mariam Mohammed Alshanqite, Hashim M ohamed Missawi. (2019). Histopathological patterns and characteristics of abnormal cervical smear in Madinah region of Saudi Arabia. Asian Pacific journal of cancer prevention: APJCP. 20(5):1303.*
9. ^a, ^b*https://prescriptec.org/. About cervical cancer in Uganda. Retrieved from https://prescriptec.org/coun tries/uganda/#:~:text=About%20cervical%20cancer%20in%20Uganda,is%2041.4%20per%20100%20 000.*

10. ^Carolyn Nakisige, Melissa Schwartz, Anthony Okoth Ndira. (2017). Cervical cancer screening and treatment in Uganda. Gynecologic oncology reports. 20:37-40.
11. a, b, cLucy O Eriba, Rukiyat A Abdus-salam, David A Dawotola. (2013). Histolopathological patterns of cervical carcinoma seen at a radiotherapy centre in Ibadan, Nigeria. Nigerian Quarterly Journal of Hospital Medicine. 23(2):125-128.
12. a, bHiralal Konar. (2016). DC Dutta's textbook of gynecology: JP Medical Ltd. ISBN 9385891596.
13. ^Syed A Hoda, Esther Cheng. (2017). Robbins basic pathology. Oxford University Press US. p.
14. ^Thangaraj Priya, Balakrishnan Indumati. (2020). Retrospective Histopathological Analysis of Cervical Cancer in a Tertiary Care Center. Journal of Evolution of Medical and Dental Sciences. 9(47):3523-3528.
15. ^Innocent O Maranga, Lynne Hampson, Anthony W Oliver, Anas Gamal, Peter Gichangi et al. (2013). Analysis of factors contributing to the low survival of cervical cancer patients undergoing radiotherapy in Kenya. PloS one. 8(10):e78411.
16. a, b, c, dVincent Vinh-Hung, Claire Bourgain, Georges Vlastos, Gábor Cserni, Mark De Ridder et al. (2007). Prognostic value of histopathology and trends in cervical cancer: a SEER population study. BMC cancer. 7(1):1-13.
17. ^American Cancer Society. (2022). Key Statistics for Cervical Cancer.
18. ^WHO. (2022). Cervical cancer facts Retrieved from https://www.who.int/news-room/fact-sheets/detail/cervical-cancer.
19. ^Crispin Kahesa, Julius Mwaiselage, Henry R. Wabinga, Twalib Ngoma, Joan N. Kalyango et al. (2008). Association between invasive cancer of the cervix and HIV-1 infection in Tanzania: the need for dual screening. BMC public health. 8(1):1-8.
20. ^Liora Newfield, H. Leon Bradlow, Daniel W. Sepkovic, Karen Auborn. (1998). Estrogen metabolism and the malignant potential of human papillomavirus immortalized keratinocytes. Proceedings of the Society for Experimental Biology and Medicine. 217(3):322-326.
21. ^E. W. Ngwalle, H. N. Mgaya, W. Mpanju-Shumbusho, Z. M. Chirenje, L. Kirumbi et al. (2001). Situation analysis for diagnosis and treatment of cervical cancer in mainland Tanzania. East African medical journal. 78(2):60-64.
22. ^Stephen E. Hawes, Cathy W. Critchlow, Papa Salif Sow, Papa Touré, Ibraham N'Doye et al. (2006). Incident high-grade squamous intraepithelial lesions in Senegalese women with and without human immunodeficiency virus type 1 (HIV-1) and HIV-2. Journal of the National Cancer Institute. 98(2):100-109.

23. a, b *A. Paloma Vizcaino, Victor Moreno, F. Xavier Bosch, Nubia Munoz, Xoan M. Barros-Dios et al. (200 0). International trends in incidence of cervical cancer: II. Squamous-cell carcinoma. International journ al of cancer. 86(3):429-435.*

Declarations

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