Life Science Journal

Websites:
http://www.lifesciencesite.com
http://www.sciencepub.net

Emails:
editor@sciencepub.net
sciencepub@gmail.com

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

Human Papillomavirus Types, 16 and 18 Among HIV Sero Positive Women Attending Aminu Kano Teaching Hospital, Kano, Nigeria

Taysir Ramadan Hafiz[1], Emmanuela C. Ngwongwo[2], Usman A Dutsinma[1]

[1] Department of Medical Microbiology and Immunology, Al-Azhar University and Bayero University Kano
[2] Department of Microbiology, Faculty of Science, Bayero University Kano, Nigeria
dr.taysiralassuty@gmail.com

Abstract: Globally, one of the mainly widespread sexually transmitted infections is the Human Papillomavirus (HPV). HPV is the most important etiologic agent in cervical tumor development. HPV types 16 and 18 are more virulent, causing more than 16% of all cervical carcinomas. An associated infection of high-risk genital HPV types with the Human Immunodeficiency Virus (HIV) representing an oncogenic problem. **Aim of the work,** To determine the prevalence of Human Papillomavirus types 16 and 18 infection among HIV sero positive women attending Aminu Kano Teaching Hospital (AKTH), Kano, Nigeria. The CD_4 counts and HIV-viral load of the subject women were obtained from their medical record. Data generated were analyzed using SPSS software version 20. This research involved 86 sexually active HIV positive women in which 25(29.1) % were single, 61(70) % were married. Their age group was between 20-50 years. 50 (58.1%) out of the 86 women enrolled in this study were positive for HPV, while 36 (41.9%) were negative for HPV. From the pap smear carried out, low squamous intra-epithelial lesion (LSIL) that were found was 17 (19.8%), atypical Squamous Cell-High Squamous intra-epithelial legion (ASC-HSIL cannot be excluded) seen were 11 (12.8%) and negative with inflammation were 38 (44.2%). From the 28 samples that have cell abnormalities, 6 (21.4%) were positive for HPV type 16, while 16 (57.1%) were positive for HPV type 18. This study shows that women living with HIV are prone to develop cervical cancer, as 28 (32.6%) out of 86 women enrolled in this study have cell abnormalities, which indicate that, there is possibility for cervical cancer occurrence. This study also shows that there is a high prevalence of Human Papillomavirus Infection, as type 16 and 18 were detected from these women. There should be an effective pap smear annual screening among women living with HIV, and early treatment of precancerous cervical lesions, to prevent cervical cancer occurrence.

[Taysir Ramadan Hafiz, Emmanuela C. Ngwongwo, Usman A Dutsinma. **Human Papillomavirus Types, 16 and 18 Among HIV Sero Positive Women Attending Aminu Kano Teaching Hospital, Kano, Nigeria.** *Life Sci J* 2020;17(2):32-39]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). http://www.lifesciencesite.com. 6. doi:10.7537/marslsj170220.06.

Keywords: Human; Papillomavirus; HIV; Sero; Positive; Women; Hospital; Nigeria

1. Introduction

One of the main widespread sexually transmitted infections is the Human Papillomavirus (HPV), with about 10% an incidence in women worldwide (De Sanjose *et al.,* 2007). HPV is considered as the chief causative agent in cervical cancer development, although most infections are asymptomatic and self-limiting (Bosch *et al.,* 2002). Different types of HPV was discovered, exceeding than 200 types have been recognized, of which 14 HPV types have been catagorized as tumrogenic depending on several sources (16,18,31,33,35,39,45,51,52,56,58,59 and 66, IAR, Group 1) or perhaps carcinogenic (68, IARC Group 2A) (IARC, 2012). HPV types 16 and 18 are more virulent, causing more than 16% of all cervical carcinomas (De Sanjose *et al.,* 2010).

The oncogenic prospective of high-risk genital HPV types may be affected with other infections such as the Human Immunodeficiency Virus (HIV) (Anastos *et al.,* 2010).

Another venereal disease which threatened the world is the Acquired Immune Deficiency Syndrome (AIDs), which caused via the Human Immunodeficiency Virus (HIV) infection. At the beginning of infection no clear symptoms can be detected on the infected person or some symptoms such as influenza-like disease signs (WHO, 2015). With the advancement of infection with HIV, an interferes further with the immunity of human being, rising the risk of most common infective viruses such as Human Papillomavirus (WHO, 2015).

HIV-related immunodeficiency and HIV positivity, estimated by low CD4 count, are identified to be connected with high frequency and occurrence of all high-risk HPV types (Palefsky, 2009), causing an elevation in the risk of invasive cervical cancer in women living with HIV and cervical intraepithelial neoplasia (CIN) (Massad *et al.,* 2015, Clifford *et al.,* 2016).

The Human Papillomaviruses (HPV) are a group of viruses including about 100 -150 strains of virus, more than forty strains can influence the genital region, mouth and throat. Persons carrying HPV has been associated with a higher risk of infection with HIV (Michael, 2013).

The strains of HPV associated with cancer include high-risk HPV 16, 18, 31, 33, 45, 52 and 58, whereas, the strains that causing genital warts are considered low-risk HPV 6 and 11, (ASHA, 2015). Where there are a differences in the strains of HPV that affecting the person and developed to warts, from that causing tumor (CDC, 2015).

According to previous research, almost all cervical tumor is caused by HPV 16 and 18 types, and representing about 70% of cases (WHO, 2016). Individuals infected with HPV develop warts, such as genital warts or certain cancers. The warts seem to be in the form of a small bump, stem-like protrusions or cluster of bumps. The shape of warts may be large, flat or cauliflower shaped and the color may be appear as white or flesh tone (CDC, 2015). The most common area affected in women include the vulva, and may be present near the anus, on the cervix or with the vagina (ASHA, 2015).

Papilloma viruses are able to live and adapted to specific cells called squamous epithelial cells. Squamous epithelial cells are present on the surface of the skin and on moist membranes such as mucosal membranes such as: vulva, cervix, anus, the vagina, mouth, inner nose, the urethra throat; and inner foreskin of the penis, and trachea and the bronchi; the inner eyelids (American Cancer Society, 2016). Individuals infected with Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDs) are at a high risk of increasing invasive tumors of the cervix, and anus, caused by Human Papillomavirus (HPV) (Massad et al., 2015).

Human Papillomavirus can be constricted through out vaginal or oral sex or unprotected anal by either close physical touch with the genital region, or by sharing sex toys, even if the infected person has no clear symptoms or signs of HPV. It is probable for a mother to pass HPV on to her baby during delivery (Michael, 2013).

Risk of HPV-associated tumors was increased between individuals suffering from AIDs and exaggerated with growing immunosuppression (Anil *et al*., 2009). HIV-positive women have a high incidence of infection with human papillomavirus (HPV), and are infected with a broader range of HPV types than women with HIV-negative (Clifford *et al*., 2006).

The occurrence of cervical and anal cancer caused by some strains of human papillomavirus is high since the introduction of antiretroviral therapy (ART) in 1996. The first hint that this might occur was the observation that, development of cervical and anal cancer were not clearly linked to development of AIDs, unlike other HIV-linked tumors like Non-Hodgkin's Lymphoma and Kaposi's Sarcoma (Frisch and Goodman, 2000). This suggest that HIV-related immunosuppression due to ART, may not lead to a decline in the incidence of anal cancer or cervical cancer. Instead, the anal cancer increases if the individuals were living longer due to ART (Palefsky *et al*., 2001). An increasing incidence of anal cancer since the introduction of ART, was reported from France using the national French Hospital Database on HIV (Piketty *et al*., 2008).

The estimation carried out by WHO, 2015, reported that the total estimated cervical cancer during 2012, was about 266,000 deaths and 528,000 new discovered cases worldwide (WHO, 2015). In recent studies, the rate of infection with HPV in Americans was about 79 million, and about 14 million cases each year are newly infected, also in the United States the incidence of cervical tumor in women yearly was more than 11,000 women (ACS, 2016).

Human Papilloma virus cannot be treated, but most can be overcome in peoples having good immune statues. The cell changes caused by HPV can be treated to prevent cancer (ACS, 2016).

Aim

To determine the prevalence of Human Papillomavirus infection among HIV sero positive women attending Aminu Kano Teaching Hospital (AKTH), Kano.

Significance of the Study

This study will go a long way in assisting in the implementation of knowledge regarding HIV and HPV co-infection, cervical cancer prevention and screening recommendations, thereby reducing the rate of HPV types 16 and 18 infections and cervical cancer occurrence.

2. Material and Methods

Study Area

This investigation was done at Aminu Kano Teaching Hospital, Kano. It is a Tertiary Government Teaching Hospital located in Kano, Kano State, Nigeria. It has about 700 beds capacity, 2,200 permanent staffs and 150 consultants in different specialties, the Hospital is well equipped with medical

facilities and it is a life saving hospital (Wikipedia, 2018).

Study Design

This study is cross-sectional study, which was conducted on HIV positive women in S.S Wali Clinic, Aminu Kano Teaching Hospital, Kano.

Ethical Clearance

Ethical approval was attained before the commencement of the research from the Aminu Kano Teaching Hospital ethical committee.

Study Population

This consists of HIV sero-positive women attending Aminu Kano Teaching Hospital, Kano.

Determination of Sample Size

The sample size for this study was determined using sample size determination in health studies $n = \frac{Z^2PQ}{d^2}$(Lwanga and Lameshow, 1991).

0.06% prevalence rate of HIV/HPV coinfection will be adopted (Cunningham *et* al., 2006)

Where:

n = Minimum sample size

Z = percentage point of standard normal distribution curve, which defines 95% confidence interval = 1.96 (constant)

P = 0.06%

Q = 1 – P

d = Maximum sampling error allowed at 95% confidence limit i.e. 0.05

Therefore Z=1.96

$$n = \frac{(1.96)^2 \times 0.06(1-0.06)}{(0.05)^2}$$
$$= 3.8416 \times 0.06 \times 0.94$$
$$= \frac{0.217}{0.0025}$$
$$= 86$$
$$\therefore n = 86$$

Inclusion Criteria

Only HIV sero-positive women attending Aminu Kano Teaching Hospital that gave consent to participate were included in this study.

Exclusion Criteria

HIV/AIDs negative women was not included in this study. HIV positive women that refused to give consent to participate were excluded.

Study Sampling Technique

Random sampling of the subjects was adopted in this study.

Method of Data Collection

Demographic data of the subjects which include age, residence, tribe, job educational background, qualifications, were gotten from the HIV clients using the questionnaire. The patient's current CD4 cells count and viral load were obtained from their medical records.

Specimen Collection and Preparation

Blood specimens were collected from 86 subjects using standard blood sample collection procedure, (Gesigner, 2010), and were put into a clean disposable container without anticoagulant, were incubated at 37^0C for 30 minutes, and were centrifuged at a speed of 4000RPM for 5 minutes, the serum were separated and put in a cry valve and were stored at -2^{o}C. Pap smears were also collected from the subjects using standard pap sample collection procedure (ACS, 2016).

Data Analysis

Data generated were analyzed using SPSS Software version 20 (2011, Corp. IBM Corp.). The prevalence of HPV infection among HIV seropositive women where expressed in simple proportions and percentages for the study groups. Chi-square was used to determine the relationship between the $CD4^+$ levels on the HIV/AIDs infected individuals that are HPV positive and those that are HPV negative.

3. Results

This research involved 86 sexually active women in which 25(29.1%) were single, 61(70.9%) were married. Their age group was between 20-60 years of age.

Table 1: Shows HPV rapid test done on the 86 serum samples collected, 50(58.1%) were positive to HPV while 36(41.9%) were non-reactive. The relationship between the HPV positive women and their age where compared and it shown that there is no significant relationship between the age and HPV status of the subjects at P value > 0.05.

Table 2: Shows the Pap Smears done on the 86 subject women, 28(32.5%) were seen to have cell abnormalities. 38(44.2%) were negative with inflammation while 20(23.2%) were seen negative. Among the 28(32.5%) that have cell abnormalities, 17(19.8%) were at the grade of Low Squamous Intraepithelial Lesion (LSIL), while 11(12.8%) were at the grade of Atypical Squamous cell- High Squamous Intraepithelial lesion (ASC-HSIL).

Table 3: Shows the relationship between the Women that are reactive with HPV rapid test, where compared with the period they have been on Anti-Retroviral Therapy (ART), it shown that there is no significant relationship.

Table 4: Shows HPV Eliza test carried out on the 28(32.5%) women that have cell abnormalities, for the detection of HPV types 16 and 18. 6(21.4%) were HPV type 16, 16(57.1%) were HPV type 18, while 6(21.4%) were neither HPV type 16 nor HPV type 18. The relationship between the sample of the women that are reactive to HPV 16 and HPV 18 were compared with their CD4count, and there is no significant difference.

Table5: Shows the relationships between the sample of the women that are reactive to HPV types 16 and 18 and their various viral load. There is no significance difference observed as the P-value is >0.05.

Table 6: Shows the relationships between the sample of the women that are reactive to HPV types 16 and 18 and their various ages. There is no significance difference observed as the P-value is >0.05.

Table 7: Shows the relationships between the sample of the women that are reactive to HPV types 16 and 18 and their various marital status. There is no significance difference observed as the P-value is >0.05.

Table 8: Shows the relationships between the sample of the women that are reactive to HPV types 16 and 18 and their various academic qualifications. There is no significance difference observed as the P-value is >0.05.

Table 4.1: Prevalence of HPV among HIV sero-positive women. Based on age

Age Group (Years)	No. Screened	Positive	Percentage	P-value
20-25	3	3	100.0	0.9704
26-30	20	11	55.0	
31-35	19	12	63.2	
36-40	17	9	52.9	
41-45	15	7	46.7	
46-50	12	8	66.7	
Total	**86**	**50**	**58.1**	

Table 4.2: Prevalence of Abnormal Cervical Cells Based on Age

Age Group (years)	No. Screened	ASC-HSIL	%	ISIL	%	Negative with Inflammation	%
20-25	3	0	0.0	1	33.3	2	66.7
26-30	20	1	5.0	3	15.0	10	50.0
31-35	19	1	5.3	5	26.3	5	26.3
36-40	17	3	17.7	1	5.9	11	64.7
41-45	15	3	20.0	2	13.3	8	53.3
46-50	12	3	25.0	5	41.7	2	16.7
Total	**86**	**11**	**12.8**	**17**	**19.8**	**38**	**44.2**

Table 4.3: Prevalence of HPV based on ART Administration

Art (years)	No. Screened	Positive	Percentage	P-value
0-5	25	21	84.0	0.5567
6-10	45	22	48.9	
11-15	12	5	41.7	
16-20	3	2	66.7	
21-25	0	0	0.0	
26-30	1	0	0.0	
Total	**86**	**50**	**66.7**	

Table 4.4: Prevalence of HPV Type 16 And 18 On Positive Smear Based On CD4 Cells Count.

CD4 Count (Cells /µL)	No Screened	HPV 16	%	HPV 18	%
>500	12	3	25.0	8	66.7
200-499	14	3	21.4	8	57.1
< 200	2	0	0.0	0	0.0
Total	**28**	**6**	**21.4**	**16**	**57.1**

Table 4.5: Prevalence Of HPV Types 16 and 18 Based On Viral Load

Viral Load (Copies/Ml)	No. Screened	HPV 16	%	HPV 18	%
0-50 (undetectable)	13	3	23.1	5	38.5
51-500	8	1	12.5	7	87.5
501-1000	1	0	0.0	0	0.0
>1000	6	2	33.3	4	66.7
Total	**28**	**6**	**21.4**	**16**	**57.1**

P-value = 0.4933

Table 4.6: Prevalence of HPV Types 16 and 18 Based on Age

Age Group (Years)	No. Screened	HPV 16	%	HPV 18	%
20-25	1	1	100.0	0	0.0
26-30	4	0	0.0	3	75.0
31-35	7	1	14.3	5	71.4
36-40	3	0	0.0	1	33.3
41-45	5	2	40.0	4	80.0
46-50	8	2	25.0	3	37.5
Total	**28**	**6**	**21.4**	**16**	**57.1**

P-value = 0.4127

Table 4.7: Prevalence of HPV Types 16 and 18 Based on Marital Status.

Marital Status	No. Screened	HPV 16	%	HPV 18	%
Single	6	3	50.0	4	66.7
Married	22	3	13.6	12	54.6
Total	**28**	**6**	**21.4**	**16**	**57.1**

P-value = 0.2632

Table 4.8: Prevalence of HPV Type 16 and 18 Based on Qualification (s)

Qualifications	No. Screened	HPV 16	%	HPV 18	%
Primary	6	1	16.7	4	66.7
Qur'anic	4	1	25.0	2	50.0
Secondary	7	0	0.0	5	71.4
Tertiary	11	4	36.4	5	45.5
TOTAL	**28**	**6**	**21.4**	**16**	**57.1**

P-value = 0.3337

4. Discussion

From the previous research, it was observed that females existing with HIV have a high incidence of infection with human papillomavirus (HPV) (Franceschis *et al*., 2006). It is remarkable that 58.1% that were seen reactive to HPV test in this research is very high. Generally, the two sexually transmitted infections HIV and HPV infection are usually accompanied each other (Strickler *et al.,* 2005). Also It is demonstrated that HIV- induced impairment in the immune system, therefore, it is possible that HPV infection will increased and become insistent in HIV-infected females (Strickler *et al.,* 2005), and progress into pre-cancerous, and cancerous lesions of the cervix of the uterus (Frisch *et al.,* 2000).

According to the International Agency for Research on Cancer (IARC, 2005), it is conceivable that HPV cooperates with HIV via enhancing gene expression of HPV or even HIV. The probable mode of action may be through, the HIV-I tat protein may convince other HPV regulatory expression.

This study also discovered that with elevated HIV heterosexual transmission and recurrent co-infection with (HPV), invasive tumors in the cervix will highly increase between HIV-infected women (Maiman *et al.,* 2005). Women with HIV have high rates of cervical abnormalities (Goldie *et al.,* 2009). This is remarkable as 28 out of 86 women involved in this study have cervical abnormalities.

the cancer may be violent and the therapy may be unsuccessful in the case of development of cervical cancer in women (Palefsky *et al.*, 2006), thereby accounting for high rates of cervical intraepithelial Neoplasia (Maiman *et al.,* 2005).

The risk of increasing cervical abnormalities appears to differ with the degree of immune suppression (Goldie *et al.,* 2009). Palefsky *et al.*, 2006, reported that the risk of HPV is more in HIV-infected females with CD4-positive lymphocyte counts (<200 cells/mm^3). Also, they added that high HIV viral loads were prognosticators of HPV infection amide HIV positive women.

The frequency of cervical tumor amide women with AIDs has not declined in spite of there is a partial effect on the immune restoration induced by anti-retraurial treatment on the national background of HPV infections, yet (Heard,2004).

Different measures can be applied for preventing cervical cancer in women such as periodic screening; early discovery and treatment of pre-invasive cervical mess which can be efficient in avoiding cervical cancer via stop their advancement into invasive

cervical tumor (Massad *et al.,* 2015). In the united states, all HIV infected women must receive cervical tumor screening by the use of Pap Smear test, twice per year post HIV diagnosis, and each year thereafter as recommended by HIV treatment guidelines issued by the US Public Health Service and the Infectious Diseases Society of America Since 1995 (Aberg *et al.,* 2004).

Stain et al., showed that in the United States 19% of HIV-infected women not delivery cervical tumor screening during the past year which are in care for HIV infection (Stain *et al.,* 2001).

Also the studies made by Breen et al., which involved large population, found that relatively high rate (14% - 20%) of women not performing cervical tumor screening along the 3 years before interviewed (Breen *et al.,* 2001).

In southern Europe, the causes for insufficient screening coverage of women exhibiting with HIV although global right to use antiretroviral drugs and, therefore, regular communication with medical services are not strong. In Italy, it looks that professionals are conscious of the present guidelines on cervical cancer screening for HIV-infected women, as reported by a survey of referral clinics for people with HIV infection, nevertheless that the difficulties met are of an organizational nature, i.e. complications in merging routine follow-up of makers for HIV Infection with genital organs of women examination which is generally done away (Murri *et al.,* 2006)

In low-resource counties cervical cancer screening programs are hard to appliance and continue for a diversity of causes, comprising lack of trained personnel, cost, low patient follow-up rates and insufficient laboratory support. On the other hand, It is impossible to perform cervical cancer screening programs for women in developing countries with low income and this can be shown from the scale-up of antiretroviral therapy in low-resource countries and most of US funds were used not only to obtain antiretroviral therapy only, but also to development of treatment infrastructure, laboratory support and offer training. Women which giving a treatment as antiretroviral therapy, would be checked on a regular basis, and are required for cervical cancer screening (PEPFAR, 2006).

Regarding high-resource countries, it is observes that the cytological screening programs have cramped greatly the incidence and mortality of cervical cancer, but in some countries e.g. Latin American Countries, in spite of widespread of cytological cervical screening, but it is difficult to obtain high standards due to obstacles in performing cytology samples which may attributed to deficient infrastructures in the laboratories, poorly collected samples, and inadequate training and supervision, and lack of follow-up procedure for abnormal findings in cytology laboratories (IARC, 2005).

Feasibility studies for cervical cancer screening in women for HIV infection in low and medium resource countries is not available particularly those concerning cost-effectiveness and clinical benefits, but in the US an investigation reported that annual papanicolaou cytological smears were accompanied with predictable life expectancy benefit equivalent to or bigger than those given by additional preventive measures in HIV or general medicine illness (Goldie *et al.*, 2009).

The lately permitted HPV vaccine, approved for use in females their ages ranging from 9 to 26 years old, may in the caring decades, lead to decline in the incidence of invasive cervical cancer and cervical cytological anomalies in HIV infected women, depending on the present observation coming from the results of HPV vaccinated females before the age of sexually maturated. Most young women, even if previously infected with some types of HPV, will received at least partial benefit from the vaccine, the vaccine is non-infectious and thus can be safety administered to women who are HIV infected, in addition to the benefits of vaccine as being more effective when received before the onset of sexual maturity (Markowitz *et al.,* 2007).

However, the disadvantages of HPV vaccine represented in non-saving protection of already HPV infected women, and the vaccine not protect against all types of HPV, even if given before infection, Therefore, it is essential to persist to carry out regular cervical cancer screening amide women who have been vaccinated (Markowitz *et al.,* 2007).

Conclusion

This study show that there is high prevalence of HPV types 16 and 18 among women living HIV infection as the result shows to be 6(21.4%) and 16(57.1%) respectively.

The current study also shows that there is high prevalence of cell abnormalities caused by human papillomavirus among women living with HIV-infection, pap smear result, it was found to be 28 (32.5%) cell abnormalities.

There is no great impact on CD4, as those with high CD4 level were infected with HPV.

Recommendations

i. It is recommended that women living with HIV should be screened for HPV infection.

ii. It is also recommended that women living with HIV should be annually screened for cervical cancer using papaniculaou test for early detection of precancerous cells and thereby prevent the occurrence of cervical cancer.

iii. HPV vaccine should be given to those that have not been infected with HPV infection.

iv. Boosting of CD4 cells count will also enhance in the reduction of HPV infection among women living with HIV.

v. Further studies is also recommended for the detection of other HPV high-risk types that are carcinogenic.

References

1. Aberg, J.A., Gallant, J.E., Anderson, J. (2004). Primary care guidelines for the management of persons infected with human immuno-deficiency virus: recommendations of the HIV medicine Association of the infectious Diseases society of America. *Clinical Infectious Disease.*39:609-629.
2. American Cancer Society, Human Papillomavirus Staining Method. April 12, 2016.
3. Anastos, K., Hoover, D.R., Burk, R.D., Cajigas, A., Shi, Q., Singh, D.K., Cohen, M.H., Mutimura, E., Sturgis, C., Banzhaf, W.C. Risk factors for cervical precancer and cancer in HIV-infected, HPV-positive Rwandan Women, PLoS ONE 2010, 5, el3525.
4. Anil, K., Chaturuedi, Margaret, M., Madeleine, Robert, J., Biggar, Eric, A., Engels. (2009). Risk of Human Papillomavirus-associated cancer among persons with AIDs. *Journal National cancer Institution* 101 (16):1120-1130. Human Papillomavirus (HPV) Resources (2015).
5. Bosch, F.X., Castellsague, X., Diaz, M., De-Sanjose, S., Hammouda, D., Shah, K.V., Meijer, C.J. (2004).*"Against which human papillomavirus types shall we vaccinate and screen? The International perspective". International Journal Cancer.*111(2): 278-85.
6. Breen, N., Wagener, D.K., Brown, M.L., (2001). Progress in cancer screening over a decade: results of cancer screening from the 1987, 1992, and 1998 National Health Interview Surveys. *Journal National Cancer Institute.*
7. CDC, what is HPV, accessed 28 May 2015.
8. Clifford, G.M., Franceschi, S., Keiser, O., Schoni Affolter, F., Lise, M., Dehler, S., Levi, F., Movsavi, M., Bouchardy, C., Wolfensberger, A. Immunodeficiency and the risk of cervical intraepithelial neoplasia 2/3 and cervical cancer: A nested case-control study in the Swiss HIV Cohort study. *International Journal Cancer* 2016, 138, 1732-1740.
9. Clifford, G.M., Goncalves, M.A., Franceschi, S. (2006) Human Papillomavirus types among women infected with HIV: a meta-analysis, AIDs, Vol. 20 (Pg. 2337-44).
10. David Cunningham 1, William H Allum, Sally P Stenning, Jeremy N Thompson, Cornelis J H Van de Velde, Marianne Nicolson, J Howard Scarffe, Fiona J Lofts, Stephen J Falk, Timothy J Iveson, David B Smith, Ruth E Langley, Monica Verma, Simon Weeden, Yu Jo Chua, MAGIC Trial Participants (2006): Perioperative Chemotherapy Versus Surgery Alone for Resectable Gastro esophageal Cancer. New England Journal of Medicine. 355 (1), 11-20.
11. De Sanjose, S., Diaz, M., Castellsaque, X., Clifford, G., Bruni, L., Munoz, N., Bosch, F.X. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: A meta analysis. Lancet Infect. Dis. 2007, 7, 453-459.
12. De Sanjose, S., Quint, W.G.V., Alemany, L., Geraets, D. T., Klaustermeier, J.E., Lioveras, B., Tous, S., Felix, A., Bravo, L.E., Shin, H.R. Human Papillomavirus genotype attribution in invasive cervical cancer: A retrospective cross-sectional worldwide study. Lancet Oncol. 2010, 11, 1048-1056.
13. Franceschi, S., Herrero, R., Clifford, G.M., (2006). Variations in the age-specific curves of human papillomavirus prevalence in women worldwide, *International Journal Cancer,* vol. 119 (pg. 2677-84).
14. Frisch, M. and Goodman M.T. (2000). Human Papillomavirus-associated carcinomas in Hawaii and the mainland US cancer; 88(6):1464-9.
15. Frisch, M., Biggar, R.J., Goedert, J.J. (2000). Human papillomavirus associated cancers in patients with human immunodeficiency virus infection acquired immunodeficiency syndrome, *Journal National cancer Institute*, vol. 92 (pg. 1500-10). Gesigner, 2010).
16. Goldie, S.J., Weinstein, M.C., kuntz, K.M., Freedberg, K.A. (2009). The costs, clinical benefits, cost effectiveness of screening for cervical cancer in HIV-infected women, Ann Inter Med, vol. 130 (pg. 97-107).
17. Heard, I., Palefsky, J.M., Kazatchkine, M.D. (2004). The impact of HIV anti-viral therapy on human papillomavirus (HPV) infections HPV-related diseases, Antivir Ther, vol. 9 (pg. 13-22).
18. International Agency for Research on cancer (AIRC) (2005). AIRC handbooks of cancer prevention, volume 10: cervix cancer screening, Lyon, France IARC press.
19. Lwanga, S.K. and Lemeshow, S. (1991). Sample size Determination in Health Studies. A practical Manual, World Healthh Organization, 2:1-3.
20. Maiman, M., Fruchter, R.G., Guyl. (2005). Human Imuno-deficiency virus infection and invasine cervical carcinoma. Cancer, 71:402-406.

21. Markowitz, L.E., Dunne, E.F., Saraiya, M. (2007). Quadrivalent human papillomavirus vaccine: recommendations of the Advisory committee on Immunization Practices (ACIP). MMWR Recomm Rep. 56 (RR-2):1-24.
22. Massad, L.S., Xie, X., D'Souza, G., Darragh, T.M, Minkoff, H., Wright, R., Colie, C., Sanchez-Keeland, L., Strickler, H.D. Incidence of cervical precancers among HIV-sero-positive women. Am, J. Obstet. Gynecol. 2015, 212, 606.el-e8.
23. Michael Carter. (2013). Human Papillomavirus (HPV) and genital Warts.
24. Murri, R., Franceschi, S., Rauizza, M. (2006). Access to gyneocological services papanicolauo tests in HIV-infected Italian women; a questionnaire survey, AIDs care, vol. 18 (pg. 376-8).
25. Palefsky, J. Human Papillomavirus-related disease in people with HIV. Curr. Opini. HIV AIDS 2009, 4, 52-56.
26. Palefsky, J.M., Gillison, M.L., Strickler, H.D. (2006). HPV vaccines in Immuno compromised women, men, vaccine, vol. 24 Suppl 3 (pg. 140-6).
27. Palefsky, J.M., Holly, E.A., Ralston, M.L., D.A., Costa, M., Bonner, H., Jay, N. (2001). Effect of highly active antiretroviral therapy on the natural history of anal squamous intraepithelial lesions and anal human papillomavirus infection. *Journal Acquired Immunodeficiency Syndrome* 28(5):422-8.
28. The U.S president's Emergency Plan for AIDs Relief (PEPFAR) Available at: Accessed December, 2006.
29. Piketty, C., Selinger-Leneman, H., Grabar, S., Duvivier, C., Bonmarchand, M., Abramawitz, L. (2008). Marbed increase in the incidence of invasive anal cancer among HIV-infected patients despite treatment with combination antiretroviral therapy. *AIDs* Jun 19: 22(10):1203-11.
30. Stein, M.D., Cunnigham, W.E., Nakazono, T. (2001). Screening for cervical cancer in HIV-infected women receiving care in the United States. *Journal Acquire Immune Deficiency Syndrome*. 27: 463-466.
31. Strickler, H.D., Burk, R.D., Fazzari, M. (2005). Natural history possible reactivation of human Papillomavirus in human Immunodeficiency virus positive women *Journal National 1 Cancer Institute*. vol. 97 (pg. 557-86).
32. W.H.O. (2016). Human Papillomavirus (HPV) and Cervical Cancer.
33. W.H.O. *(2015). "WHO Model list of Essential Medicines (19th list)"*
34. Wikipedia (2018). Aminu Kano Teaching Hospital.

2/9/2020