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Genotyping of Human Papilloma Virus (HPV) in Cervical Cancer at the Federal Teaching Hospital Ido-Ekiti, Ekiti State, Nigeria

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ABSTRACT

Background: Human papillomavirus (HPV) is the main causative agent of cervical cancer and 99.7% of cervical cancer has been attributed to infection by the virus. Cervical cancer is a common cancer in women in sub-Saharan Africa and it remains a serious public health issue. This study was carried out to determine the genotypes of HPV in archival specimen of cervical cancer cases at the Federal Teaching Hospital Ido-Ekiti (FTHI), Ekiti state, Nigeria.

Methods: The materials for this study consisted of paraffin embedded tissue blocks, Haematoxylin and Eosin (H&E) stained slides, hospital request forms, patients case notes and duplicate copies of histopathology reports of histologically-diagnosed cervical cancer patients at the Morbid Anatomy and Histopathology Department of FTHI between January 2017 and December 2019. DNA extraction and quantification was done. Real time PCR (qPCR) was done to determine different types of Human papilloma virus present in archival specimens using specific primers (4X HPV 28 A TOM (Primer A) and 4X HPV 28 B TOM (Primer B).

Results: Twenty-eight (28) cervical cancers were diagnosed and confirmed in the department during the study period, however, twenty-seven (27) of the cases were considered appropriate for HPV detection after histological evaluation and Twenty-five (25) (92.6%) were positive for HPV DNA. The six most common types of HPV occurring recurrently among HPV positive cases were HPV16 (47.1%), HPV35 (11.8%), HPV31 (9.8%), HPV18 (5.9%), HPV45 (3.9%) and HPV58 (3.9%). Multiple infections were detected in 68% of the cases.

Conclusion: The high occurrence of HPV type 16 in this study confirms the role of HPV 16 in cervical cancer pathogenesis in the studied population and high rate of multiple infections also suggests that multiple infections play significant role in the pathogenesis of cervical cancer. The findings of high occurrence of HPV 35 as a co-infection with HPV 16 and other types of HPV also suggest that the vaccines currently used as preventive measures against cervical cancer in this environment which offers no prevention against HPV 35, may not prevent majority of invasive cervical cancers in the studied population.

INTRODUCTION

Human papillomavirus (HPV) was designated an oncogenic virus following the demonstration of its DNA in cervical cancer from many countries around the world[1]. Infection by the virus is one of the most common sexually transmitted infections in the world[2], and more than hundred HPV types have been identified, over forty of which can infect the genital tract primarily through sexual transmission. The infection may be unnoticed after clearance by body immune system, however, the persistence of HPV infection with high oncogenic risk is a condition for the occurrence of cervical precancerous and cancerous lesions[3]. When the precancerous lesions are not treated, some are likely to progress into cancer

It is universally accepted that human papillomavirus (HPV) is the necessary cause of cervical cancer with more than 99% of Invasive cervical cancer containing the DNA of the virus[4]. HPV is sexually transmitted and the majority of infections occur in adolescents or young adults with the highest prevalence observed in the 15 to 19-year-old group[5]. Spontaneous viral clearance is observed in most cases within a year and time of clearance likely depends on HPV genotype. It has been observed, for example, that HPV 16 persisted longer than other genotypes[6]. HPV persistence represents the major risk factor for cervical cancer[7, 8].

With an incidence estimated at about 530,000 new cases and 275,000 deaths worldwide each year[9]. Cervical cancer is the leading cancer in women in sub-Saharan Africa and it remains a serious public health issue. It represents the fourth most common malignancy in women around the world[10], and the second most common cancer, next to breast cancer in Nigeria[11].

In developed countries, with effective and extensive screening with Pap smears, it is usually possible to identify and treat asymptomatic precursor lesions of cervical cancer, making it nearly 100% preventable[12]. However, five out of six women with cervical cancer live in developing countries, and 80% of them are diagnosed at advanced stages[13].

About 15 Human papilloma viruses, known as high risk types have been associated with invasive cervical cancer[1]. Among these high risk types, HPV types 16 and 18 were found to predominate and involved approximately 70% of cancers of the cervix in the world[14]. Prophylactic vaccines based on HPV 16/18 L1 virus-like particles (VLP) are now available[15, 16], but accurate geographical data on HPV type distribution are essential for predicting their impact. Studies have shown some variation in the serotypes among different populations[1, 17]. This difference in the distribution of genotypes was found in women who were living in different regions of the same country[18]. In Burkina Faso, the study conducted by[19], as a follow up to two previous studies in Ouagadougou[20, 21], showed that the most common high-risk HPV genotypes were HPV 35 and HPV 52.

Vaccination against HPV has been found as effective means of primary prevention of cervical cancer[22]. HPV vaccines protect against two to seven high-risk strains of the virus and may prevent up to 90% of cervical cancers[23]. Three HPV vaccines are already approved for use; these are Cervarix (a bivalent vaccine against HPV16 and HPV18), Gardasil (a tetravalent against HPV6, 11, 16, and 18), and Gardasil 9 (9-valent vaccine against HPV6, 11, 16, 18, 31, 33, 45, 52, and 58).

Despite, the high incidence of cervical cancer in Nigeria, there are only a few large-scale population-based studies on HPV prevalence and genotype distribution reported from this region[24, 25], and very few from archival cervical cancer samples[26].

A study done in Ido Ekiti, Ekiti State detected HPV in abnormal cervical cytology smears and showed high prevalence of HPV DNA[27]. However, no data is available on previous study to assess the prevalence and distribution of HPV genotypes in archival cervical cancer specimen at the Federal Teaching Hospital Ido-Ekiti.

MATERIALS AND METHODS

This was a three-year retrospective study involving the analysis of histologically diagnosed cervical cancer patients at the Histopathology Department of Federal Teaching Hospital (FTH) Ido-Ekiti, Ekiti State, Nigeria between January 2017 and December 2019. The study included only cases of cervical specimens received and histologically diagnosed as Invasive cervical cancer. Demographic data of patients were obtained from the hospital case files and laboratory forms.

Materials and data collection

The materials included hospital request forms, referral cards, patients case notes, duplicate copies of histopathological reports that were issued within the study period and archival tissue blocks and corresponding archival slides.

Archival slides of the diagnosed cervical cancer were retrieved and reviewed to determine and confirm the histologic types of cervical cancer. Fresh sections from the tissue blocks were taken in situations where the original slides were not found or had been damaged. Appropriate Formalin fixed paraffin embedded (FFPE) tissue blocks for DNA extraction were retrieved and selected from the archive.

Formalin fixed paraffin embedded (FFPE) tissue samples were sectioned at 2 microns from tissue blocks using a microtome and deparaffinization was done using 400 µL of deparaffinization solution (Zymo quick DNA kit) and the solution was thereafter removed by decantation. DNA extraction with freshly prepared 10 µL of Proteinase K and purification were done using Genomic DNA tissue kit (Zymoresearch, USA). Nanodrop spectrophotometry was used for DNA

quantification, this was carried out in order to determine the concentration of DNA present in the mixture, as well as the purity.

CFX96^{TM} Real-time PCR machine was used for the genotyping of the HPV DNA. The PCR was done following laboratory guidelines and protocols using Seegene Anyplex HPV 28 Detection kit (Seegene, Seoul, South Korea) which composed of two primers, 4X HPV 28 A TOM (Primer A) and 4X HPV 28 B TOM (Primer B) to detect 28 HPV DNA, EM1 (Master Mix), RNase- free water, three (3) Positive control (PC1, PC2 and PC3) and an Internal control (IC). These primers detect 28 genotypes which include the high-risk and low-risk HPV genotypes, with each primer set detecting 14 genotypes. Primer A detects HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, and internal control (IC); while Primer B detects 5 types of high risk and 9 types of low risk which include; HPV6, 11, 26, 40, 42, 43, 44, 53, 54, 61, 69, 70, 73, 82, and internal control (IC). Each Positive control includes clones for 5 targets in set A, and 5 targets in set B. The dyes used in the Seegene Anyplex HPV 28 Detection kit were five in number, and they include: FAM (Fluorescein amidite), HEX (Hexachloro-fluorescein), Cal Red 610, Quasar 670, and Quasar 705. Each dye fluorescence for 3 HPV types from each primer set.

Two sets of cocktails A and B were prepared with Set A containing 5 µL of 4X HPV 28 A TOM (primer A), 5 µL of EM1 and 5 µL of RNase- free water, making a total of 15 µL in each test tube. Set B cocktail containing primer B (4X HPV 28 B TOM) was also prepared similarly in different test tubes. Thereafter, 5 µL of each DNA sample was added to the set A and B tubes containing the 15 µL of the PCR master mix, with each tube labeled 1 to 27 respectively for set A and set B. Also 5 µL of each positive control HPV 28 PC1, PC2 and PC3 were added to separate cocktail test tubes of cocktail set A and set B. A negative control was also prepared for each cocktail set by adding 5 µL of RNase-free water to two test tubes each containing cocktail set A and set B respectively (The control samples were provided by the manufacturer). After completing the cocktail preparation, then the real-time PCR instrument was set up for subsequent loading of the cocktail.

The CFX96^{TM} Real-time PCR system consisted of an automatic qPCR machine and a computer monitor. The system setup program and procedure for the detection of 28 types of HPV and Internal control (IC) composed of three different steps as follow; Protocol setup, Plate setup and start run. The CFX96 PCR machine has a menu used to open the protocol editor through which protocol setup was done. Firstly, the temperature adjustment was done by selecting the appropriate temperature for each step of the cycles. This consisted of 1 to 20 steps in 50 cycles and each step has its temperature and duration preset. The steps consisted of denaturation at 95 ^{O}C in 30 cycles, annealing at 55 ^{O}C in 10 cycles and then extension at 70 ^{O}C in 10 cycles. The plate compartment of the machine was automatically opened for loading of samples into the wells, the plate consisted of 96 wells, each well was assigned for a named sample (27 samples each for set A and set B), positive control (3 each for set A and set B) and negative control (1 each for set A and set B). The samples were carefully loaded into the wells of the plate to prevent cross contamination, covered with optical strip cap and then placed in the instrument and the lid was automatically closed. Thereafter, the Fluorophores icons representing FEM, HEX, Cal Red 610, Quasar 670 and Quasar 705 were selected to specify the fluorophores to be detected in the selected wells (The fluorescence of fluorophores at melting point was indicative of HPV DNA detection). The samples, positive controls and negative controls were appropriately designated for reading and identification on the monitor. The data capture system of the PCR was programmed and the DNA genotypes and analysis was recorded in the Excel sheet. The melting point in the procedure occurred at temperature of 55 ^{O}C and 85 ^{O}C and this occurred at steps 8, 14 and 20 of the 50 cycles during which fluorescence was detected.

Statistical analysis: All the data retrieved were entered into Microsoft Excel and data analysis was performed using Statistical Package for Social Sciences version 21 (SPSS 21). One-way ANOVA was used to determine significant difference between groups while Hierarchical Loglinear analysis was used to determine association between variables. Values were considered significant at $p \leq 0.05$.

Ethical consideration: Ethical approval for the study was obtained from the Research and Ethical committee of Federal Teaching Hospital (FTH) Ido-Ekiti. The permission of the Head of Department of Histopathology, Federal Teaching Hospital (FTH), Ido-Ekiti was obtained for the use of the archival materials and other departmental materials where applicable. Furthermore, this study was conducted in accordance with the guidelines of the Helsinki declaration on biomedical research in human subjects. Confidentiality of the identity of the patients and personal health information was maintained.

RESULTS

Twenty eight (28) cases were histologically confirmed as cervical cancer during the study period, out of which one (1) case had its FFPE tissue block badly damaged which made it not appropriate for HPV DNA extraction, thus, twenty seven (27) cases were available for HPV DNA genotyping. HPV DNA were detected in twenty five (25) of the FFPE tissue blocks, representing 92.6% of the cervical cancer cases. Distributions of HPV DNA by age groups are shown in Table 1. The age group 40-49 years has the most frequent HPV DNA occurrence, accounting for 28.0% of the cases seen, followed by age group 50-59 years, accounting for 24.0% and 70-79 age group (20.0%). The subjects were 57.40 ± 14.83 (32 -82) years old with modal age of 40 – 49 years and weighed

55.22 ± 6.04 (45 – 66)Kg. They were multigravida, having given birth for 1 – 7 times (Table 1). Information on patients' educational and marital statuses, history of HPV vaccination, use of contraceptives, diabetes mellitus, hypertension, vaginal discharges and metastasis are provided in Table 1. Detection of HPV DNA from FFPE tissues obtained from the patients were not found to be significantly associated with any of their biodata (Table 1). However 100% samples of patients with diabetes mellitus, hypertension, vaginal discharges and metastasis, as well as those on oral contraceptives were positive to HPV-DNA. Samples from all the five patients that had earlier received Human papillomavirus vaccination were all positive for HPV DNA.

Table 1: Socio-Demographic pattern of cervical cancer and its relation to HPV frequency distribution

Characteristics		Frequency	Hpv DNA negative	Hpv DNA positive	Significance (p value)
Age (years)	30-39	3	1 (33.3)	2 (66.7)	0.412
	40-49	7	0 (0)	7 (100)	
	50-59	6	0(0)	6 (100)	
	60-69	3	0 (0)	3 (100)	
	70-79	6	1 (16.7)	5 (83.3)	
	≥ 80	2	0 (0)	2 (100)	
Weight (Kg)	≤ 49	6	1 (20.0)	5 (80.0)	0.221
	50-59	13	0 (0)	13 (100)	
	≥ 60	8	1 (12.5)	7 (81.5)	
Education	No formal education	12	1 (8.3)	11 (91.7)	0.718
	Primary	1	0 (0)	1 (100.0)	
	Secondary	8	1 (12.5)	7 (87.5)	
	Graduate	6	0 (0)	6 (100.0)	
Marital status	Single	0	0 (0)	0 (0)	0.836
	Married	22	2 (9.1)	20 (80.9)	
	Divorced	0	0 (0)	0 (0)	
	Widow	5	0 (0)	5 (100.0)	
Parity	1	0	0 (0)	0 (0)	0.643
	2	3	0 (0)	3 (100.0)	
	3	5	1 (20.0)	4 (80.0)	
	4	4	0 (0)	4 (100.0)	
	5	8	0 (0)	8 (100.0)	
	6	5	1(20.0)	4 (80.0)	
	7	2	0 (0)	2 (100.0)	
Diabetics	No	23	2(8.7)	21 (91.3)	0.535
	Yes	4	0 (0)	4 (100.0)	
Hypertension	No	22	2 (9.1)	20 (90.9)	0.355
	Yes	5	0 (0)	5 (100.0)	
Usage of oral contraceptive	No	22	2 (9.1)	25 (90.9)	0.479
	Yes	5	0 (0.0)	5 (100.0)	
Hpv vaccination	No	22	2 (9.1)	20 (90.9)	0.915
	Yes	5	0 (0)	5 (100.0)	
Vaginal discharges	No	9	0 (0)	9(100.0)	0.192
	Yes	18	2 (11.1)	16 (88.9)	
Metastasis	No	20	2 (10.0)	18 (90.0)	0.263
	Yes	7	0 (0)	7 (100.0)	

Percentages in parenthesis

Table 2 shows specific types of Human papilloma virus DNA distribution in cervical cancer cases as single and or multiple infections. Among the HPV DNA positive cases, single HPV type infection was identified in eight samples, representing 32% of the cases. All the single infections were due to HPV16. Multiple HPV infections were found in seventeen samples, constituting 68% of the cases. In all the multiple infections, HPV16 and HPV35, HPV16 and HPV31 occurred together most frequently and recurrently, accounting for 24.0% and 20.0% of the multiple infections respectively, while HPV16 and HPV18 accounted for 12.0% of multiple infections. The six most common HPV types occurring recurrently among samples were HPV16 (47.1%), HPV35 (11.8%), HPV31 (9.8%), HPV18 (5.9%), HPV45, (3.9) and HPV58 (3.9%). Others were HPV types 26, 42, 43 52, 56, 59, 68, 69 and 73 (Table 2). It was noted that HPV16 was identified in 24 of the 27 samples (88.9%) tested for HPV DNA, occurring both as single infection and as a multiple infection (Table 2).

Table 2: Distribution of Human papilloma virus as single/mixed infections in cervical cancer

HPV types	Frequency	%
Single type		
HPV16	8	32.0
Multiple type		
HPV16, 18	2	8.0
HPV16, 31	3	12.0
HPV16, 35	3	12.0
HPV16, 42	1	4.0
HPV16, 43	1	4.0
HPV16, 58	1	4.0
HPV35, 58	1	4.0
HPV16, 45, 73	1	4.0
HPV16, 18, 31, 35	1	4.0
HPV16, 31, 35, 52	1	4.0
HPV16, 26, 56, 69	1	4.0
HPV16, 45, 59, 68	1	4.0

KEY: % - Percentage

Table 3 shows distribution of human papillomavirus types by histological types of cervical cancer. HPV DNA was more frequently seen in squamous cell carcinoma, followed by adenocarcinoma and poorly differentiated carcinoma. HPV16/HPV35 (HPV16 as single infection plus HPV16 and HPV35 as co-infection) accounted for a 58.8% of the HPV positive invasive cervical cancer cases by histologic type. Majority of the cases with multiple infections were squamous cell carcinoma. HPV16 was the most common type identified in squamous and adenocarcinoma cases (Table 3), It was identified either in single/multiple infections in eighteen (18) cases and five (5) cases of the squamous and adenocarcinomas respectively. HPV35 was found in six (6) samples of squamous cell carcinomas, while HPV31 accounted for four (4) cases of squamous cell carcinoma. The only case of poorly differentiated carcinoma contained HPV16 and HPV45. No HPV DNA was detected in one (1) case of adenoid cystic carcinoma seen. However, it was only HPV16 that showed significant association in its frequency distribution in histologic types of cervical cancer ($p = 0.050$).

Table 3: Distribution of Human papillomavirus subtypes among cervical cancer histological types

HPV subtype	SCC	AC	ACC	PDC	Total	p value
HPV 16	18	5	0	1	24	0.050*
HPV18	2	1	0	0	3	0.889
HPV 26	1	0	0	0	1	0.869
HPV 31	4	1	0	0	5	0.939
HPV 35	6	0	0	0	6	0.079
HPV 42	1	0	0	0	1	0.887
HPV 43	0	1	0	0	1	0.381
HPV 45	1	0	0	1	2	0.710
HPV 52	1	0	0	0	1	0.852
HPV 56	1	0	0	0	1	0.861
HPV 58	2	0	0	0	2	0.689
HPV 59	0	0	0	1	1	0.855
HPV 68	0	0	0	1	1	0.867
HPV 69	1	0	0	0	1	0.861
HPV 73	1	0	0	0	1	0.861

KEY:
SCC - Squamous cell carcinoma
AC - Adenocarcinoma
ACC - Adenoid cystic carcinoma
PDC - Poorly differentiated carcinoma
*Significant

Figure 1 shows the histologic spectrum of cervical cancers seen in this study, squamous cell carcinoma was the commonest, it accounted for 20 cases (71.4%), it was followed by adenocarcinoma, which consisted of 6 cases (21.4%), adenoid cystic carcinoma and poorly differentiated carcinoma were 1 case each (3.6%).

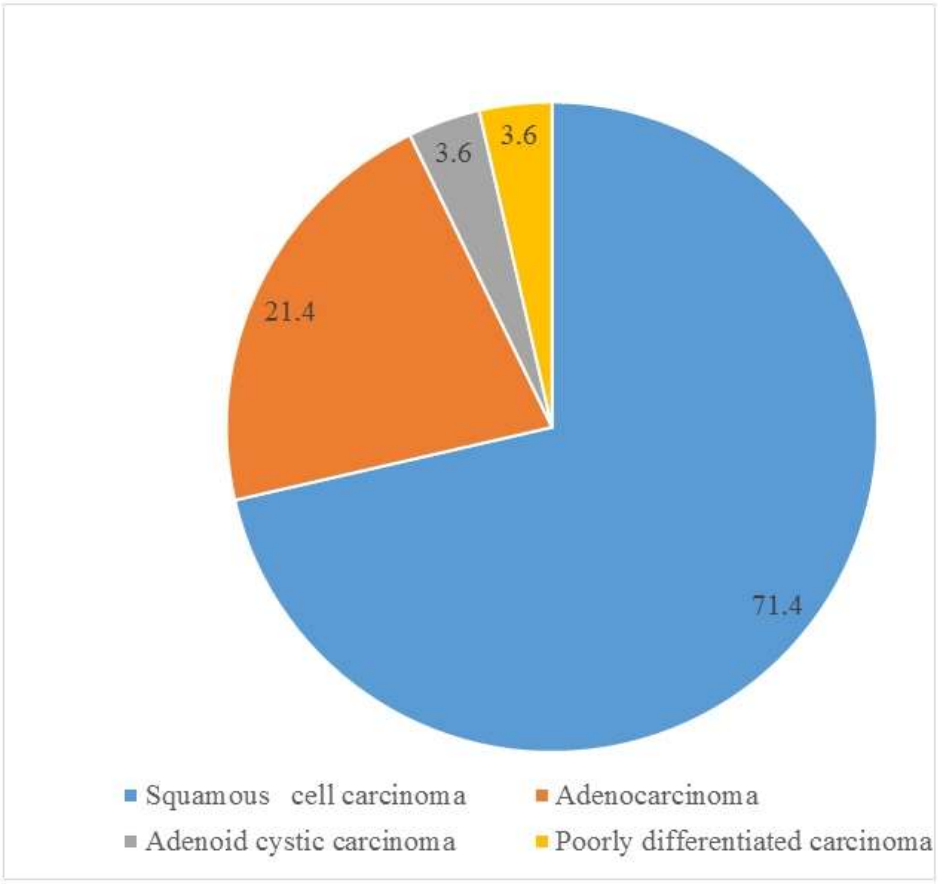

Figure 1: Distribution of histologic types of cervical cancer (Values in percentages)

DISCUSSION

Human papillomavirus (HPV) is one of the viruses causing cancerous diseases. It is sexually transmitted and high-risk HPV DNA is found to be present in 99.7% of cervical cancer specimens [4]. The vast majority of HPV infections is transitory and become undetectable in 12–24 months after infections[28, 29]. However, in some women whose infections continue to persist, the risk of developing precancerous conditions is significant. Many studies confirmed that persistent infection with an oncogenic HPV type is the main risk factor for causing a cervical intraepithelial neoplasia (CIN) that may range from CIN1 to CIN3 and cervical cancer[30, 28, 31]. In this study, HPV DNA was detected in 25 of the 27 cervical cancer samples analyzed, giving an overall prevalence rate of 92.6%. This is comparable to other studies from around the world, where prevalence rates of 95 and 96% from India and Italy were recorded respectively[32, 33], and higher than that of finding from Uganda and Lagos, Nigeria which recorded prevalence of 61.3% and 82.6% respectively[34, 26]. The higher occurrence of HPV DNA in this study supports and confirms the importance of HPV infection in the development of cervical cancer.

The HPV type 16 was the most common virus worldwide with prevalence rates accounting for 32.3% of all infections in Southern Asia, 28.9% in Southern Europe, 24.4% in Western Europe, 24.3% in Northern America, and 12% in Africa[35]. HPV16 and HPV18 are recognized as the main causes of invasive cervical cancer and its precursor lesions. These two viral types were found in most cases of cervical cancer from 22 countries around the world[1]. HPV16 was the most prevalent and recurring type in this study, accounting for 47.1% of all the infections as a single and part of multiple infections. This is consistent with findings from several other studies that showed HPV16 as the most prevalent HPV in cervical cancer specimen and in the general population[34, 33, 26].

Most of the infections in this study were due to mixed infections by HPV genotypes occurring in 17/25 (68%) of samples. This is comparable, though higher than findings from studies in Zimbabwe, Italy and France, where high percentage of multiple infections in patients were found, accounting for 18%, 22.2%, and 24% of cases respectively[36, 37, 38]. However, it was significantly higher than findings from studies in Egypt, Uganda and Lagos which reported 0.02%, 3.7%, and 4.4% respectively for mixed HPV infection in invasive cervical cancers[39, 34, 26]. It was noted that mixed infections (68%) in this study were greater than mono infection (32%), this was at variance with what was reported in the literature where single infection with HPV was usually greater than the mixed infections[34, 33, 26].

This could be due to a smaller proportion of samples when compared to these other studies. This could also be an emerging trend of this infection in causing cervical cancer. However, further studies involving a larger sample size or a cross sectional multicenter studies involving a larger population are required to confirm this. Among the histological specimens that contained HPV DNA, 32% (8/25) were mono-infected. It was noted that all the single infections were by HPV16. This is consistent with findings from several other studies that showed HPV16 as the most prevalent HPV in cervical specimen and in the general population [1].

It should be noted that multiple infections have been found to have an impact on treatment outcomes, it was also associated with risk of treatment failure and therefore, had to be followed up for response and suitable interventions done for a favorable outcome[40], multiple infections have been found to be associated with increased cervical cancer risk[41].

Multiple infections in this study shown that HPV16 and HPV35, HPV16 and HPV31 were found in 5 samples each followed by HPV16 and HPV18 (3 cases) with an additional HPV35 and HPV58 co-infection found in one sample, these findings were at variance to reports from other studies[38, 42, 34, 26], that showed that major proportion of co-infections in cervical cancers were due to HPV16 and HPV18. Study in Burkina Faso[43], showed that the most common high-risk HPV genotypes were HPV39 (18.5%), HPV52 (16.7%), HPV18 (14.8%), and HPV35 (13.0%), HPV16 which has been reported to be the most prevalent in cervical cancer was not found in the population studied. The finding of higher HPV types 16 and 35 as well as HPV types 16 and 31 co-infection in this study was not in consonance with a metanalysis which found HPV types 16 and 18 to be the most common among African women[44]. This underlies the importance of geographical variability of the virus and it should be noted that HPV35 which was detected in high proportion in this study is not yet covered by any of the available vaccines. Whether multiple HPV infections are the mainstay in cervical cancer pathogenesis is still unclear, a study in Costa Rica found that the risk of cervical cancer associated with HPV16 alone is similar or greater than the risk associated with multiple infections (HPV16 plus other HPV types)[45], and another study elsewhere found multiple infections were associated with increased cervical cancer risk[41]. Although the number of cases in this study was rather small, the results have some important implications. If the HPV vaccines available presently containing 16 and 18 antigens are close to 100% efficacy[46, 16], then one could assume that about 60% of cervical cancer cases would not be prevented by the use of the vaccine.

Squamous cell carcinoma is the most common histologic variant in this study, this is consistent with findings in Lagos[47] and also in other parts of Nigeria[48, 49]. This study demonstrated the dominance of HPV16 in invasive squamous cell carcinoma and adenocarcinoma, this is consistent with the findings in the studies done in France and Lagos, Nigeria[38, 26]. However, this is not in consonance with the studies in Uganda and Netherland that demonstrated dominance of HPV18 in adenocarcinoma[50, 34]. A study in Colombia, South America attributed 93% of adenocarcinoma cases to HPV types 16, 18, and 45[51]. Also found in higher proportion in the squamous cell carcinoma in this study were HPV35 (15.4%) and HPV31 (10.3%), this is similar to some other studies which demonstrated the presence of HPV31 and HPV35[34, 26], and it should be noted that HPV35 is not yet included in any of the available vaccines.

The only adenoid cystic carcinoma identified in this study did not contain any HPV DNA. Adenoid cystic carcinoma is a malignant tumor that exceptionally occurs in the uterine cervix. It is mostly seen in postmenopausal women and has an aggressive clinical course[52]. Integrated high risk HPV genomes, in particular type 16, have been detected in this uncommon type of primary cervical cancer[53]. Therefore the absence of HPV DNA in the adenoid cystic carcinoma in this study may be due to the smaller sample size studied.

CONCLUSION

The occurrence of HPV DNA in archival samples of cervical cancer from Federal Teaching Hospital Ido-Ekiti, Ekiti State, Nigeria was 92.6 % supporting its role in the aetiopathogenesis of cervical cancer in this region.

The results of this study confirm the role of HPV 16 in cervical cancer pathogenesis at the Federal Teaching Hospital Ido-Ekiti, Ekiti State, Nigeria. The results suggest that multiple infections play significant role in the pathogenesis of cervical cancer and with the high occurrence of HPV 35 in the multiple infections, this suggests that the current vaccines being used as preventive measures against cervical cancer in this environment which does not protect against HPV 35, could not possibly prevent a significant part of invasive cervical cancers. It is thus, advised that screening for cervical intraepithelial lesion should be continued after vaccination.

In view of varied geographical distribution of HPV types and HPV35 which was not included in any of the available vaccines occurred in high proportion in this study, it is thus recommended that future vaccines should be tailored according to local HPV type distribution[26].

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Conflicts of interest:

We declare no conflicts of interest.

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