

# Predictors of Knowledge, Attitude And Uptake Of Human Papilloma Virus Vaccine Among Adolescents In Bauchi Local Government Area Of Bauchi State, Nigeria

Abubakar Musa,<sup>1</sup> Usman Abba,<sup>2</sup> Yusuf Isa Isa,<sup>3</sup> Kauthar Suleiman Ochwu,<sup>3</sup>  
Abdulrahman Shu'aibu,<sup>3</sup> Muhammad Bashir Jibril,<sup>4</sup>  
Mohammed Kabir Abdullahi<sup>5</sup>

Department Of Community Medicine, Abubakar Tafawa Balewa University And Abubakar Tafawa Balewa  
University Teaching Hospital, Bauchi - Nigeria

Ministry Of Health Damaturu, Yobe State - Nigeria

College Of Medical Sciences, Abubakar Tafawa Balewa University, Bauchi - Nigeria

Department Of Community Medicine, Amadu Bello University, Zaria - Nigeria

Department Of Obstetrics And Gynaecology, Abubakar Tafawa Balewa University And Abubakar Tafawa  
Balewa University Teaching Hospital, Bauchi - Nigeria

## Abstract

**Background:** Cervical cancer is a vaccine preventable disease, it remains a public health issue, with the disease's highest burden seen in developing countries such as Nigeria, where it is the second most frequent gynecological cancer and is associated with high morbidity and mortality. It is caused by HPV infection, which is a vaccine preventable sexually transmitted infection with high incidence among the younger population. This study assessed knowledge, attitude and Uptake of HPV Vaccination among adolescents in Bauchi Local Government Area of Bauchi State.

**Methods:** A descriptive cross-sectional study was employed using semi-structured interviewer administered questionnaire to 422 female adolescents of Bauchi Local Government Area, Bauchi State. Responses were collated and analyzed using SPSS version 23.0 and the level of significance is set at 0.05.

**Results:** the mean age and SD of the respondents are  $13.0 \pm 2.0$  and majority are Hausa by tribe (62%), Muslims (98%), with secondary level of education (47%), single (100%), not engaged in menial works (70%). There was good knowledge on HPV vaccine (65%), good attitude towards HPV vaccine (99.3%) and also good uptake of the HPV vaccine (60%) among the respondents. Also, the factors from the study that contribute significantly to the knowledge of HPV vaccine was level of education of the respondents and that of uptake of HPV vaccine were age and ethnicity of the respondents but, none was significant for attitude. Formal education, age and ethnicity were the predictors of knowledge of, and uptake of HPV infection and vaccination among the respondents.

**Conclusion:** Adolescents within the age of 9 to 14 years in Bauchi LGA, Bauchi State have good knowledge, attitude and uptake of HPV infection and vaccine. Age, level of education and ethnicity of the respondents are the factors associated with good knowledge, and uptake of HPV infection and vaccine but, none was significant for attitude. The predictors of knowledge of, and uptake of HPV infection and vaccine of the respondent were age, formal education and ethnicity. There is need to strengthen the HPV vaccination among adolescent to prevent the infection and its consequences.

**Keywords:** Knowledge, attitude, vaccine uptake, HPV, Bauchi

Date of Submission: 08-10-2024  
18-10-2024

Date of Acceptance:

## I. Introduction:

Human papillomavirus (HPV) infection is globally recognized as one of the most prevalent sexually transmitted infections and the primary causative agent of cervical cancer. It is noteworthy that over 50% of sexually active females experience lifetime exposure to at least one HPV type. While HPV can affect women of all age groups, the highest incidence of infection is observed in the 20 to 24 age bracket. It is a significant fact that nearly all sexually active men and women will contract at least one type of HPV during their lifetimes.

Notably, a substantial number of new HPV infections are reported annually in both men and women in Africa. Furthermore, it is pertinent to mention that HPV is considered a major carcinogenic factor, classified as a group 1 carcinogen according to the criteria of the International Agency for Research on Cancer. Various high-risk HPV types are causally associated with approximately 5% of all cancers, 10% of female cancers, and 16% of cancers in women in countries with limited resources.<sup>1</sup>

Cervical cancer ranks as the second most prevalent cancer among women globally and stands as the third most common cancer overall, irrespective of gender. Shockingly, over 80% of the 274,000 annual cervical cancer-related deaths occur in developing nations, with this figure projected to escalate to 90% by 2020. Beyond its impact on cervical cancer, the human papillomavirus (HPV) is causally linked to a substantial percentage of cancer cases, including 90-93% of anal cancer cases, 12-63% of oropharyngeal cancer cases, 36-40% of penile cancer cases, 40-64% of vaginal cancer cases, and 40-51% of vulvar cancer cases.<sup>2</sup>

The types of HPV are classified as high or low risk based on their potential to progress to malignancy and their association with genital warts. High-risk HPVs, such as HPV16 and HPV18, are linked to cervical cancer, constituting approximately 70% of cases. Conversely, low-risk HPVs, including types 6 and 11, are primarily associated with genital warts. The prevalence of HPV is particularly high in developing and underdeveloped countries, possibly due to inadequate healthcare systems, contributing to elevated rates of maternal and child mortality. Notably, over 90% of cervical cancer cases occur in Africa, with an estimated 569,847 new cases and 311,365 deaths annually. HPV vaccines have the potential to prevent nearly 70% of invasive cervical cancer cases globally. Women who have not received the HPV vaccine are susceptible to contracting the virus. Given the widespread prevalence of HPV as a sexually transmitted disease, it is imperative to educate women about the benefits of vaccination and the risks associated with non-vaccination. Insufficient awareness of the dangers of HPV and the consequences of non-immunization may lead to enduring health complications from HPV.<sup>3</sup>

In 2020, an estimated 12,100 new cases of cervical cancer and 8,000 deaths were reported in Nigeria. This places cervical cancer as the second leading cause of cancer-related morbidity and mortality among Nigerian women, following breast cancer. The statistics are particularly alarming as an estimated 60.9 million Nigerian women aged 15 years and older are at a heightened risk of developing cervical cancer if effective and affordable prevention and early detection strategies are not widely implemented. This underscores the urgent need for comprehensive and accessible healthcare interventions to address this significant public health challenge in Nigeria.<sup>4</sup>

The identification of HPV as the primary cause of HPV-associated malignancies has provided us with valuable opportunities to effectively control and manage these cancers through the development of vaccines and other therapeutic approaches. Vaccines have long been utilized as a preventive measure against infectious diseases, and the successful development of prophylactic HPV vaccines targeting the major capsid protein L1 of the viral particle has been a significant achievement. While prophylactic vaccines have proven effective in preventing HPV infections and re-infections, they are unable to address established HPV infections and associated lesions. In response, therapeutic HPV vaccines have emerged as a promising method to treat and eliminate existing HPV infections and related diseases. Unlike prophylactic vaccines, therapeutic HPV vaccines are designed to stimulate cell-mediated immune responses, specifically targeting and eliminating infected cells.<sup>5</sup> The prophylactic HPV vaccine has been authorized in over 100 countries since 2006. Currently, three types are available: the 9-valent HPV Vaccine (Gardasil9, 9vHPV) providing protection against strains 6, 11, 16, 18, 31, 33, 45, 52, and 58; the Quadrivalent HPV vaccine (Gardasil, 4v HPV) providing protection against strains 6, 11, 16, and 18; and the Bivalent HPV vaccine (Cervarix, 2v HPV) providing protection against strains 16 and 18. These vaccines are manufactured by Cervarix (GlaxoSmithKline Biologicals, Belgium), Gardasil (Merck & Co., USA), and Gardasil9 (Merck & Co., USA).<sup>6</sup>

Research has demonstrated that vaccination can effectively reduce the occurrence of reproductive tract diseases in both females and males. These diseases include anal and oral HPV infection, as well as cervical, vaginal, vulvar, penile, and anal intraepithelial neoplasia. Since the issuance of the vaccine license, there has been a significant global decrease in HPV infection and related incidence rates. The World Health Organization has thoroughly confirmed the safety, efficacy, and long-term effectiveness of the prophylactic HPV vaccine. This confirmation underscores the potential for vaccination to effectively control the occurrence of HPV-associated cervical cancer in human populations.<sup>7</sup>

In 2006, both the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) endorsed the administration of the Human Papillomavirus (HPV) vaccine to individuals of both sexes. This vaccine is typically prescribed to females aged 12 to 26 in three doses over a six-month period. It has proven to be an effective primary preventive measure against cervical cancer. Its usage has been associated with a reduction in HPV-related illnesses, malignancies, and HPV genotype prevalence, without any documented adverse effects.<sup>8</sup>

The available data suggests that the effectiveness of HPV vaccination is more pronounced at younger ages. It has been demonstrated that administering the vaccine at age 12 or 13 yields significantly better results than doing so at age 14 or 15, and both are more effective than vaccinating later in adolescence and early adulthood. Anticipated outcomes indicate that vaccinating individuals aged 9 to 11 will likely be equally effective in preventing infections with vaccine-type HPV, pre-cancers, and HPV-attributed cancers as vaccinating at age 12 or 13, and is expected to elicit a more robust immune response.<sup>9</sup>

Cervical cancer has a profound impact on the global female population, affecting in excess of 500,000 women annually. Notably, it disproportionately affects women in low- and middle-income countries (LMICs), where nearly 90% of cervical cancer-related deaths occur. Globally, it ranks as the fourth most common cause of cancer-related deaths in women, and stands as the primary cause of such deaths in women across eastern, western, middle, and southern Africa. Nigeria plays a significant role in the overall burden of cervical cancer. The country reports an incidence rate of approximately 18.4 cases per 100,000 women, with an estimated 12,075 new diagnoses annually. Consequently, cervical cancer stands as the second leading cause of female cancer-related deaths in Nigeria. The unequal distribution of cervical cancer cases and associated mortality is closely tied to disparities in access to secondary prevention. Countries with robust screening programs have achieved a notable 50% reduction in cervical cancer-related deaths.<sup>10</sup>

Cervical cancer prevention encompasses specific interventions, including health education on delayed sexual debut, the practice of safe sex, and the benefits of HPV vaccination, as well as prophylactic vaccination against HPV. Early diagnosis is crucial, and complete cure is possible through screening methods such as the Papanicolaou (Pap) smear test. Regrettably, the adoption of both HPV vaccination and cervical screening services remains rudimentary in Nigeria. It is advised that girls aged 9 to 15 years should receive a two-dose regimen of the HPV vaccine with a 6-month interval between doses (0, 6 months) before sexual activity initiation. Women aged 16 to 26 years can receive a 3-dose regimen (0, 1, and 6 months or 0, 2, and 6 months), necessitating cervical cancer screening post HPV vaccination. Notwithstanding the availability of HPV vaccination as the primary preventive method against cervical cancer, a decline in HPV infections is anticipated. However, despite advancements in HPV vaccination and education, over half a million women worldwide develop cervical cancer annually, with over 85% of cases occurring in developing countries due to ineffective screening and prevention programs.<sup>11</sup>

The introduction of the HPV vaccine in Nigeria in 2009 has not led to significant awareness, knowledge, or uptake among the target population of young people. A decade later, there persists a concerning lack of understanding regarding HPV as the causative agent of cervical cancer and the preventive benefits of HPV vaccination. This is evidenced by the unfavorable attitudes demonstrated by many parents, adolescents, and youths towards the vaccine. The low awareness, knowledge, and uptake of the HPV vaccine among Nigerians have remained persistent challenges since its introduction.<sup>12</sup>

The World Health Organization (WHO) has issued a Call to Action for the eradication of cervical cancer. In response, key stakeholders, including donors and governments, are making significant efforts to prioritize cervical cancer in their public health plans and budgets. The elimination of cervical cancer hinges on the widespread implementation of HPV vaccination as a primary prevention measure and the establishment of screening programs for the early detection and treatment of precancerous lesions as a secondary prevention strategy. It is crucial to emphasize that even as countries introduce the HPV vaccine, regular screening remains vital for both vaccinated and unvaccinated women. To achieve a decrease in the incidence of cervical cancer, it is imperative that screening coverage reaches 70% of eligible women.<sup>13</sup>

It's tragic that a woman dies every two minutes from cervical cancer, especially given the advancements in its prevention and treatment. Although cervical cancer can largely be prevented through HPV vaccination and screening, its incidence is rising annually, exacerbating global health inequalities. In terms of worldwide cancer statistics, cervical cancer is the fourth most common, with approximately 604,000 new cases and 342,000 deaths reported in 2020.<sup>14</sup> It's concerning that around 90% of global cervical cancer cases and deaths occur in low- and middle-income countries (LMICs), with women of lower socioeconomic status suffering the most. These disparities highlight significant socioeconomic differences between countries and unequal implementation of cervical cancer prevention measures, such as HPV vaccination and screening programs. Therefore, it is a moral imperative to address the significant inequities in cervical cancer burden and prevention efforts, particularly in LMICs. HPV types 16 and 18 are responsible for 66.9% of invasive cervical cancers. In Nigeria, the situation for women of reproductive age (15 to 45 years) is particularly troubling, with an estimated 12,075 new cases annually as of 2020, making cervical cancer the second most common cancer among women. Additionally, HPV types 16 and 18 infections are expected to be found in 3.5% of women with cervical cancer.<sup>4</sup> Very few studies have examined adolescents' knowledge about HPV and its vaccines. Consequently, understanding the prevalence and determinants of this knowledge among young people in Nigeria would be highly beneficial for public health. Such information would greatly assist the Nigerian government and other stakeholders in developing, promoting, and implementing public health policies and

programs aimed at reducing the spread of HPV in the community and encouraging vaccine uptake among adolescents.<sup>15</sup>

Examining the uptake of the HPV vaccine is vital for several reasons. It helps evaluate the effectiveness of vaccination programs in preventing HPV-related diseases, such as cervical cancer, which is a significant health issue in Nigeria. Additionally, it identifies barriers to vaccination, including lack of awareness, cultural beliefs, and misinformation, enabling policymakers to address these issues and improve vaccination rates. Enhancing HPV vaccination in Nigeria also supports global efforts to reduce health disparities and achieve universal access to essential vaccines, contributing to global health equity preventing HPV infection and its consequences.

## **II. Methods**

### **Study Area**

Bauchi State is located in the North-eastern geopolitical zone of Nigeria 10.30°N 10.00E°. <sup>42</sup> Based on the 2006 census, which found that the population of Bauchi State was 4,653,066 with a 3.6% growth rate, the projected population in 2023 was 8,670,000 with 3.88% growth rate. Bauchi LGA was projected to have 881,600. Bauchi LGA has 12 wards including; Dan'Iya, Birshi/Miri, Dan'amar, Majidadi A&B, Galambi, Dawaki, Zungur wards, Makama A&B.<sup>42</sup>

### **Study Design**

A community based cross-sectional descriptive study was employed.

### **Study Population**

The study population was adolescents between 10 to 14 years living in Bauchi Local Government Area for at least six months and excluded those that weren't around during the study.

### **Sample size determination**

The required sample size was obtained using an appropriate statistical formula for estimating minimum sample size in descriptive health studies; i.e.  $n = Z^2pq/d^2$  Where, n = sample size, Z = Critical value corresponding to 95% confidence interval=1.96, d= precision or accuracy = 5% = 0.05, P= prevalence of knowledge from previous study =47.6% = 0.476<sup>30</sup>

In anticipation of 10% non-response, the sample size was 422.

### **Sampling Technique**

Multistage sampling technique was employed with four stages for this study.

**Stage One:** Selection of wards, out of the 12 wards in Bauchi LGA 25% of them was selected (Makama A, Dawaki Ward, Makama B).

**Stage Two:** Out of the 3 Wards, 25% of the settlement was selected from each selected Ward.

**Stage Three:** House numbering was done in each selected settlement to obtain the sampling frame, and then sampling interval was calculated.

**Stage Four:** Selection of Respondent, after calculating the sampling interval, the first respondent was selected using simple random sampling by balloting and then subsequent respondents were selected by adding the sampling interval to the first sampled respondent. The process continued until the minimum sample size was exhausted. The respondent who gave consent and satisfied the eligibility criteria was interviewed.

### **Study Instruments**

An interviewer administered questionnaire that contains both open and closed ended questions, which was adapted from a similar study conducted in university of Lagos. The questionnaire contains 4 sections. The sections include; Section A: Socio-demographics, Section B: knowledge of HPV Infection and Vaccine, Section C: Attitude towards HPV Vaccine and Section D: Uptake of HPV vaccine.

### **Data Management**

#### **Measurement of Variables**

Dependent variables are: Knowledge, attitude and uptake of HPV infection and Vaccine

Independent variables are: Age, marital status, level of education, tribe, address, income and religion.

The Questions on knowledge about HPV infection and vaccine was dichotomized into “Yes” or “No” responses, and then scored and graded using a system adapted from a past study, where one point (1) was awarded for correct answer and zero/no point (0) was given for wrong answer or skipped question. The total score for correct answers were ten points (10). Respondents with total score of 50% and above were graded as having good knowledge while those with total score less than 50% were graded as having poor knowledge about HPV infection and vaccine.

Respondents' answers regarding attitude of HPV vaccine was graded using 5 Likert scale. 1. Strongly disagree, 2. Disagree, 3. Neutral 4. Agree, 5. Strongly agree. Scores of the correct answers were total of 25 points. Respondents with score of 50% and above of the total points were graded as having good attitude while those with score of less than 50% of the total points were graded as having poor attitude on HPV vaccine.

Respondents' answers regarding uptake of HPV vaccine was graded using 5 Likert scale. 1. Strongly disagree, 2. Disagree, 3. Neutral 4. Agree, 5. Strongly agree. Scores of the correct answers was total of 30points. Respondents with score of 50% and above of the total points were graded as having good uptake while those with score of less than 50% of the total points were graded as having poor uptake on HPV vaccine.

**Data Analysis**

Data obtained was checked for completeness, sorted, coded, appropriately cleaned and validated to ensure accuracy and consistency. The data was transferred into SPSS Version 23.0 for analysis.

Quantitative variables were summarized using mean and standard deviation (S.D) whereas categorical variables were summarized using percentages, charts and in tabular forms where necessary, To test for association of independent and dependent variables, Pearson’s Chi-square or fisher’s exact test was used with significance level at 95% confidence interval, p-value of < 0.05 was considered statistically significant. Variables that are significant at bivariate level were subjected to Logistic Regression.

**Ethical Consideration**

Ethical clearance was obtained from the Medical Research Ethics Committee of Bauchi State Ministry of Health, Bauchi (Approval Number: NH REC/TR/BAU-HREC/28/8/2023) and permission was obtained from the Bauchi LGA. Informed consent was sought from all the study participants before carrying out the study. Where respondents consented by signing the form before the questionnaire administration. Respondents were guaranteed of confidentiality of the information given and anonymity.

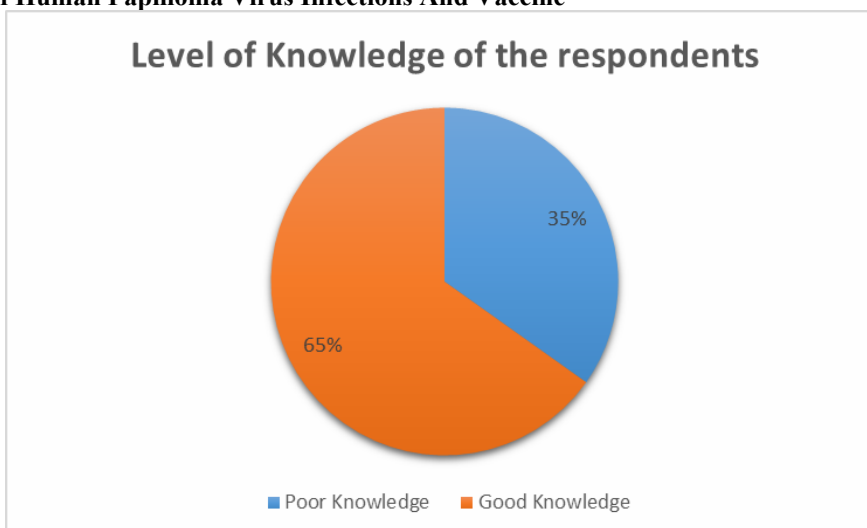
**III. Results**

**Table 1: Socio-demographic characteristics of the respondents**

Variables	Frequency (n=422)	Percentage (%)
-----------	-------------------	----------------

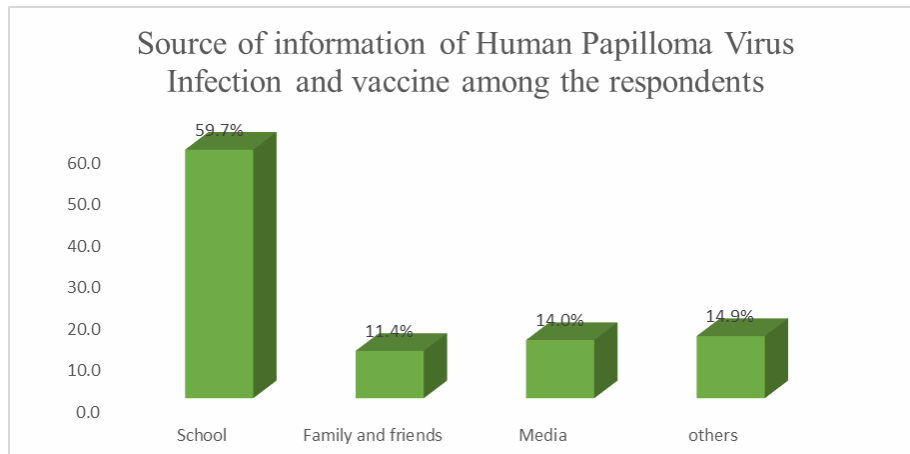
The above result show that respondents between the age of 9 – 11 years are 31.5% and between the ages 12 – 14 years are 68.5% with 47% had secondary level of education, 46% in primary level of education, 4% have are illiterate and 3% have non-formal education. The above result shows that 62% of the respondents are Hausa, 24% are Fulani, 1.9% is Yoruba, 0.5% is Igbo and 12% are from other tribes.

**Knowledge Of Human Papilloma Virus Infections And Vaccine**



**Figure 1: knowledge of HPV Infections and Vaccine among the respondents**

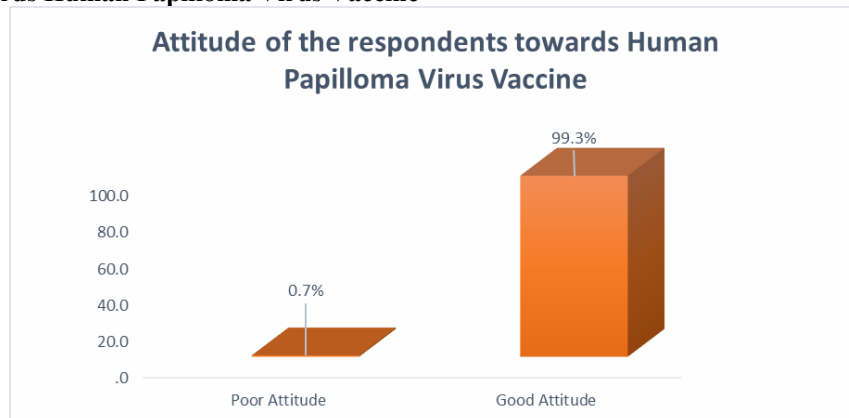
The above diagram shows that 65% of the respondents have good knowledge of Human Papilloma Virus Infections and Vaccine while 35% of them have poor knowledge Human Papilloma Virus Infections Vaccine.



**Figure 2: Sources of information of Human Papilloma Virus Infection and Vaccine among the respondents**

It shows that majority of the respondent's with a percentage of 59.7% have their source of information from school, 14.9% from other sources, 14% from the media while the least respondents with a percentage of 11.4% got theirs from Family and friends

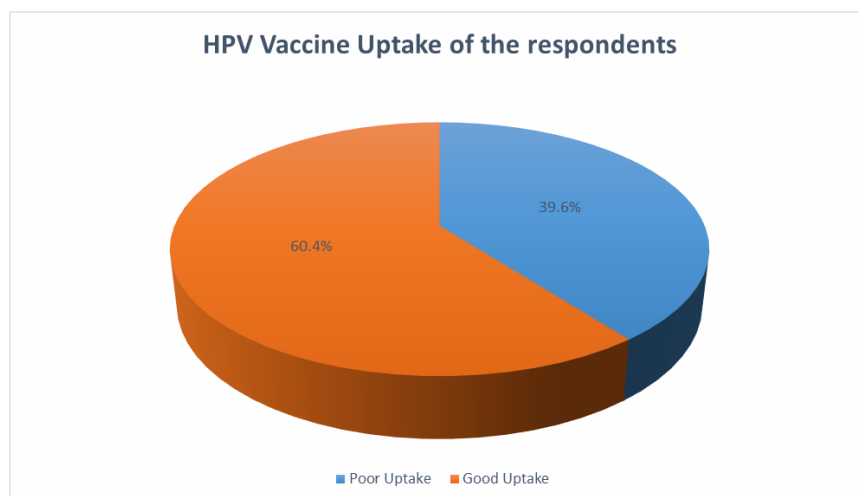
**Attitude Towards Human Papilloma Virus Vaccine**



**Figure 3: Attitude of respondents towards HPV Vaccine**

The above chart shows that 99.3% of the respondents have positive attitude towards Human Papilloma Virus vaccine while 0.7% have poor attitude towards it.

**Uptake Of Human Papilloma Virus Vaccine**



**Figure 4: Uptake of HPV Vaccine by the respondents.**

The above diagram shows that there is a 60.4% good uptake of Human Papilloma virus vaccine and a 39.6% poor uptake of human papilloma virus vaccine.

**Table 2: Factors associated with knowledge of the respondents on Human Papilloma Virus Infection and vaccine among the respondents**

Variables	Good Knowledge (%)	Poor Knowledge (%)	Total	X <sup>2</sup>	p-value
<b>Age</b>					
9 -11	83 (62.4)	50 (37.6)	133 (100)	0.652	0.442
12 -14	192 (66.4)	97 (33.6)	289 (100)		
<b>Level of Education of the respondents</b>					
Non-Formal	0 (0.0)	15 (100)	15 (100)	29.095	<b>&lt;0.001</b>
Formal	275 (67.6)	132 (32.4)	407 (100)		
<b>Religion</b>					
Islam	271 (65.0)	146 (35.0)	417 (100)	0.491	0.662
Others	4 (80.0)	1 (20.0)	5 (100)		
<b>Ethnicity of the respondents</b>					
Hausa/Fulani	229 (63.4)	132 (36.6)	361 (100)	3.296	0.081
Others	46 (75.4)	15 (24.6)	61 (100)		

The above table shows that respondents with formal level of education have good knowledge of Human Papilloma Virus infection and vaccine with a percentage of 67.6% than those respondents with non-formal level of education which is statistically significant with a p-value of < 0.001.

**Table 3: Factors associated with attitude of the respondents towards Human Papilloma Virus vaccine**

Variables	Good attitude (%)	Poor attitude (%)	Total	χ	p-value
<b>Age</b>					
9 -11	132 (99.2)	1 (0.8)	133 (100)	0.005	>0.990
12 -14	287 (99.3)	2 (0.7)	289 (100)		
<b>Level of Education</b>					

<b>of the respondents</b>					
Non-Formal	14 (93.3)	1 (6.7)	15 (100)	7.816	0.103
Formal	405 (99.5)	2 (0.5)	407 (100)		
<b>Religion</b>					
Islam	414 (99.3)	3(3)	417 (100)	0.036	>0.990
Others	5 ( 100)	0 (0.0)	5 (100)		
<b>Ethnicity of the respondents</b>					
Hausa/Fulani	358 (99.2)	3 (0.8)	361 (100)	0.511	>0.990
Others	61 (100)	0 (0.0)	61 (100)		

The above table shows the factors that are associated with the attitude of respondents towards HPV vaccine having no socio demographic variables that is statistically significant.

**Table 4: Factors associated with the uptake of Human Papilloma Virus vaccine**

Variables	Good Uptake (%)	Poor Uptake (%)	Total	$\chi$	p-value
<b>Age</b>					
9 -11	99 (74.4)	34 (25.6)	133 (100)	6.971	<b>0.010</b>
12 -14	246 (85.1)	43 (14.9)	289 (100)		
<b>Level of Education of the respondents</b>					
Non-Formal					
Formal	15 (100)	0	15 (100)	3.471	0.084
	330 (81.1)	77 (18.9)	407 (100)		
<b>Religion</b>					
Islam	342 (82.0)	75 (18.2)	417 (100)	1.605	0.227
Others	3 (60.0)	2 (40.0)	5 (100)		
<b>Ethnicity of the respondents</b>					
Hausa/Fulani	307 (85.0)	38 (62.3)	361 (100)	18.10	<b>&lt;0.001</b>
Others	54 (15.0)	23 (37.7)	61 (100)		

The above table shows that respondents with between the ages of 12 – 14 years have good uptake of Human Papilloma virus vaccine with 85.1% than respondents between the ages of 9 – 11 years with 74.4%. This is statistically significant with a p-value of 0.010. Also, the Hausa/Fulani ethnic group with 85% have good uptake of Human Papilloma virus vaccine than other tribes with 54%. This is statistically significant with a p-value of < 0.001.

**Table 5: Logistic regression showing predictors of knowledge of Human Papilloma Virus infection and vaccine**

Variable	Odd Ratio	95% CI	p-value
<b>Level of Education of the respondents</b>			
Non-Formal	1		
Formal	2.083	1.7 – 2.6	<b>&lt; 0.001</b>



The result shows that respondents with formal education are 2 times more likely to have good knowledge of HPV infection and vaccine than respondents with non-formal level of education. This is statistically significant with a p-value of <0.001.

**Table 6: Logistic regression showing predictors of Uptake of Human Papilloma Virus vaccine**

Variables	Odd Ratio	95% CI	p-value
<b>Age</b>			
9 -11	0.34	0.2 – 0.5	<b>&lt; 0.001</b>
12 -14	1		
<b>Ethnicity of the respondents</b>			
Hausa/Fulani	0.17	0.1 – 0.2	<b>&lt; 0.001</b>
Others	1		

The above table shows that respondents between the ages of 9 to 11years are 66% less likely to have good uptake of HPV vaccine than respondents between the ages of age 12 to 14 years as this is statistically significant with a p- value of < 0.001. Also, Hausa /Fulani ethnic group has 83% less likelihood of having good uptake of Human Papilloma Virus vaccine than other ethnic groups as the result is statistically significant with a p-value of < 0.001.

#### IV. Discussion

This study assessed the level of knowledge, attitude and uptake of HPV vaccine among female adolescents between the ages of 9 to 14 years in Bauchi LGA, Bauchi State. The study has shown that majority of the respondents (68.5%) are between the ages of 12 to 14 years followed by those of age of 9 – 11 years (31.5%) with standard deviation  $13 \pm (2)$ . All the respondents (100%) are single which reflects to the age group that was selected as it is highly unlikely to have married women within that age group. The respondents that are engage occupationally is (29.6%) and the ones not engaged (70%). Hausa tribe (62%) constitutes above half of the respondents, Fulani (24%), (1.9%) are Yoruba, (0.5%) are Igbo and (12%) are from other tribes. The result also shows that (98%) of them are Muslims while others is (2%). This is as most likely as a result of the predominance of Hausa and Islam in Northern Nigeria. Conversely, (47%) of the respondents have secondary levels of education, while (46%) have primary level of education, and (7%) have non-formal level of education. Meanwhile, in Bauchi, similar study was carried out in secondary schools where it shows a slightly higher mean age (SD) of the respondents 16.4 ( $\pm 2.0$ ) years, though, (56.0%) were male and (44%) are females. (34.9%) were from the Yoruba ethnic group, (56%) were from the Hausa ethnic group schooling in Bauchi State.<sup>15</sup>

Findings from our study reveal that there is good knowledge of HPV infection and vaccination (65%) among female adolescents in Bauchi Local Government Area, Bauchi State. This is in contrast to the interventional study conducted in Kano State, in which there was high proportion of the respondents with poor knowledge of HPV infection and vaccine in the intervention and control community (26.3% and 22.3%) respectively.<sup>43</sup> This is in keeping with another study done in Gombe State Tertiary Institutions where respondents (73.1%) were found to have poor knowledge about the HPV vaccine.<sup>44</sup> Also another study was conducted in University of Lagos, which shows poor knowledge among female respondents where only (3%) of the respondents had good knowledge of HPV and the vaccine.<sup>39</sup> However, majority of the respondents (92.7%) express good attitude towards uptake of HPV vaccine which is in keeping with our study which expresses (99%) good attitude towards HPV vaccine. This may be linked to the improved advocacy campaigns by the federal government in which Bauchi State is among the few States in the country that were selected by the federal government to participate in the pilot free vaccination campaigns for children between the ages of 9 to 14 years. This initiative have incorporated state healthcare agencies, media outlets and schools to execute such task. This effort clearly reflects in our research as while assessing their knowledge, it was discovered that about (59.7%) of the respondents knew about HPV in schools and (14%) of them from the media outlets. Also, most of our respondents are in secondary schools (47%) and primary schools (46%) respectively. This is in contrast to a survey conducted in Rivers state where it was found out that increasing class level is not significantly associated with the knowledge of HPV vaccine.<sup>31</sup> This is also not consistent to what was observed in similar studies, Florida and Malaysia where television/radio is their main source of information.<sup>4</sup> The study shows most of the respondents with formal level of education (**67.6%**) know that cervical cancer can be prevented by HPV vaccine which is in contrast with similar study among Northern Nigerian female students and among Italian adolescents. Both reported low level of knowledge of HPV infection and its vaccine. Also, our study is not in keeping to what was observed from a study conducted in South Africa, Kuala Lumpur and Nepal where majority of the respondents (**88.2%, 73.7%, & 88.7%**) respectively didn't know that cervical cancer can be

prevented by HPV vaccine.<sup>45</sup> Report from Port Harcourt also noted low level of knowledge of HPV and HPV vaccine among undergraduates and even lower level of knowledge among ante-natal mothers. These were two female groups who were older than our participants and were expected to have better knowledge of both HPV infection and the Vaccine.<sup>31</sup> In contrast to these findings, studies with similar design on adolescents' knowledge of HPV and its vaccine in Canada, Spain, and Germany showed increased knowledge among study participants.<sup>46</sup> The difference here is the studies were carried out in developed countries where well planned government funded immunization schedules have been in existence for a decade or more in majority of the countries. Findings from this study shows that, the higher the level of education, the more the level of knowledge on HPV and HPV vaccination. Respondents with formal level of education have better knowledge (**67.6%**), compared to those with non-formal (**26.3%**) this is similar to the study conducted in university in Lagos state, Nigeria and also a similar study conducted in Brazil.<sup>47</sup>

The findings of this study shows that almost all the respondents have good attitude towards HPV vaccine (99.37%). This is in contrast to the study done among school students in Kano State which shows poor attitude towards HPV vaccination, where (81%) of the respondents are not ready to be administered the HPV vaccine.<sup>15</sup> Also, the results across the continents have consistently shown good attitude towards HPV infection and Vaccine in high income countries compared to LMIC. Although, one of the very few results that reported otherwise came from Cameroon, a low income country. For the Cameroon study, however, it was discovered that the researchers carried out massive sensitization and educational exercises for the girls and their parents before the survey. The vaccines were also donated free for the survey. This must have accounted for the high level of attitude of the adolescent participants in their survey.

The factors associated with the attitude towards HPV vaccine also improves with higher academic level (99.5%) for the respondents with formal level of education, this finding is in contrast to a study conducted among female secondary students in Ibadan Nigeria, with very low attitude due to lack of awareness about HPV vaccine.<sup>35</sup> In the developed countries, HPV has been long incorporated into their national vaccination program. Meanwhile in Nigeria HPV vaccine has been introduced into its routine immunization schedule in October 2023 which has already taken effect coupled with the free HPV vaccination initiative initiated by the Federal Ministry of Health. There is strong link between parental approval and willingness to receive HPV vaccine. This study showed that certain variables influences the use of HPV vaccine among respondents. (41.2%) agreed that they need family and friends approval before getting vaccinated, (27.5%) believe that they strongly need approval from family and friends before getting vaccinated, (15.9%) are neutral towards that, and (13.7%) disagree with family and friends approval before getting vaccinated. Parental consent remains a key factor for the administration of medicines or vaccines to adolescents globally. However, study carried out in Rivers shows that parents that were provided with information on HPV did seem to have improved knowledge about HPV but this increased knowledge had little effect on the acceptability of these vaccines by parents for their children. Instead, attitudes and life experiences seemed to be more important factors influencing HPV vaccine acceptability among parents.<sup>31</sup>

An interesting finding from this research was that, there was very high level of vaccine uptake among the respondents which also in keeping with them having good knowledge. This is very important aspect because prevention of HPV infection is essential for the prevention of cervical cancer through HPV vaccine uptake. From the study, respondents (100%) of them are single showing good uptake of (60%) and poor uptake of (40%). This is in contrast to the study done in Gombe State Tertiary Institutions, where there was only (3.7%) who received at least one dose of the vaccine. The study showed that uptake of HPV vaccine among the respondents was very low<sup>44</sup>. So also, the Hausa/Fulani tribe shows good uptake (85%) compared to other tribes (15%). Nonetheless, this was significantly lower than a study conducted among female adolescents in Taiwan (91%) and in Scotland (94.4%).<sup>48</sup> From our study, our respondents that are not vaccinated (**48.1%**) are willing to get vaccinated which is lower than the studies done in Rivers state were majority (**71.7%**) of the girls were willing to be vaccinated against HPV. This shows they appreciate preventive measures against diseases. This result is similar to the results of the studies by Dempsey, Pelucchi, and Di Giuseppe, who reported high rates of willingness to be vaccinated with HPV vaccine.<sup>28</sup>

This is also in contrast to study conducted in Turkey, where only (43.5%) of adolescent girls received the vaccination. In the United States, (60%) of adolescent girls have received one or more doses of the HPV vaccine, according to the Centre for Disease Control. In Los Angeles, only (25%) of college students initiated the vaccine in 2012, while in Denmark, only (24%) of young women received the vaccine.<sup>49</sup> Also, our study shows that those that received single dose is (69.8%), (25%) received 2 doses and (4.7%) have completed their doses. This is almost consistent with research done in LMIC worldwide, which shows an estimated 3.3 million females received at least one dose of HPV vaccine with (**61.69%**) of the target population vaccinated between 2008 to 2020. In countries with high uptake, compared to routine programs, the estimate was higher when delivered through demonstration programs (**89.94% vs 59.74%**).<sup>50</sup>

The disparities between the findings and earlier studies could be attributed to vaccine accessibility, as some nations have higher access coverage. Also the percentage of our respondents (81%) have received the vaccine while (19%) of the respondents have not received the HPV vaccine totally compared to study carried out in Benin, Nigeria where approximately (3.7%) of the respondents had received the vaccine. Similarly, a study of female medical students at an Indian university revealed that just 6.8% of the participants had been vaccinated against HPV. Conversely, comparable research carried out in certain developed countries such as Germany and the United States reported a considerable uptake of HPV vaccines of 53% and 62.4% respectively.<sup>8</sup>

The study shows that (12.8%) of our respondents have experienced barriers in getting HPV vaccine compared to a study carried out that was aimed to evaluate the predictors and uptake of HPV vaccination and testing among urban women in Lagos, Nigeria. Findings revealed that several factors impeded the uptake of HPV vaccination, including the fear of the vaccine, lack of awareness about its availability, negative recommendations by acquaintances, and the absence of recommendations by healthcare providers.<sup>39</sup> Additionally, high costs and non-affordability were identified as major barriers. Our study clearly reflects a tremendous improvement by the health care agencies and the government towards combatting those barriers. The respondents have good uptake of Human Papilloma virus vaccine with (60%) good uptake. Also, the Hausa/Fulani ethnic group with (85%) have good uptake of Human Papilloma virus vaccine than other tribes with (54%). This is in contrast to study done that shows Hispanic, Asian, and African-Caribbean girls were even less likely to have received the full course of vaccination, indicating a potential need for targeted interventions to achieve equitable coverage.<sup>34</sup>

The need to increase HPV information dissemination through schools, media and family remain a key factor towards ensuring good knowledge, attitude and uptake of HPV vaccine among adolescents in Nigeria, as the majority of respondents claimed that they received information about HPV vaccine through schools, media and family, and also require parental approval before taking the vaccine.

The World Health Organization proposed that HPV vaccination be included in national Immunization programs, which Nigeria has recently done that, thereby, reducing the cervical cancer burden in the country at the moment and in years to come.

Finally, it is critical that health care agencies and practitioners focus on efforts to enhance HPV awareness, treatment, and prevention thereby reducing HPV infection and related complications.

## V. Conclusion

The study has shown that there is good knowledge, attitude and uptake of Human Papilloma Virus infection and vaccine among female adolescents between the ages of 9 to 14 years in Bauchi Local government Area, Bauchi State. The Level of education among the respondents was a factor associated with good knowledge of HPV infection and vaccine. Also, age (12 – 14 years) among the respondents was a factor associated with HPV vaccine uptake but none was significant for attitude. The predictors of knowledge of, and uptake of HPV infection and vaccine of the respondent were age, formal education and ethnicity.

## References

- [1] Bonanni P, Bechini A, Donato R, Capei R, Sacco C, Levi M, Et Al. Human Papilloma Virus Vaccination: Impact And Recommendations Across The World. *Therapeutic Advances In Vaccines*. 2015 (1):3–12.
- [2] Onowhakpor Ao, Omuemu Vo, Osagie OI, Odili Cg. Human Papilloma Virus Vaccination: Knowledge, Attitude And Uptake Among Female Medical And Dental Students In A Tertiary Institution In Benin-City, Nigeria. *Journal Of Community Medicine And Primary Health Care*. 2016;28(2):101–8.
- [3] Rabiu I, Yahuza Z. Knowledge And Attitude Towards Human Papilloma Virus Infection, Vaccines, And Cervical Cancer Prevention Among School Students In Kano, Nigeria. Muniraju M, Editor. *Advances In Virology*. 2023 2023:1–10.
- [4] Ezechi O, Akinsolu F, Salako A, Abodunrin O, Adewole I, Olagunju M, Et Al. High-Risk Human Papillomavirus Infection Among Nigerian Women: A Systematic Review And Meta-Analysis. *J Int Med Res*. 2023 (7):03000605231182884.
- [5] Yang A, Farmer E, Wu Tc, Hung Cf. Perspectives For Therapeutic Hpv Vaccine Development. *J Biomed Sci*. 2016 (1):75.
- [6] Burdette Am, Webb Ns, Hill Td, Jokinen-Gordon H. Race-Specific Trends In Hpv Vaccinations And Provider Recommendations: Persistent Disparities Or Social Progress? *Public Health*. 2017;142:167–76.
- [7] Zhou X, Sun L, Yao X, Li G, Wang Y, Lin Y. Progress In Vaccination Of Prophylactic Human Papillomavirus Vaccine. *Front Immunol*. 2020 11:1434.
- [8] Alkalash Sh, Alshamrani Fa, Alamer Eha, Alrabi Gm, Shaynawy Hm. Parents' Knowledge Of And Attitude Toward The Human Papillomavirus Vaccine In The Western Region Of Saudi Arabia. 2022;
- [9] Saslow D, Andrews Ks, Manassaram Baptiste D, Smith Ra, Fontham Eth, The American Cancer Society Guideline Development Group. Human Papillomavirus Vaccination 2020 Guideline Update: American Cancer Society Guideline Adaptation. *Ca A Cancer J Clinicians*. 2020 (4):274–80.
- [10] Hofman R, Van Empelen P, Richardus Jh, De Kok Im, De Koning Hj, Van Ballegooijen M, Et Al. Predictors Of Hpv Vaccination Uptake: A Longitudinal Study Among Parents. *Health Education Research*. 2014;29(1):83–96.
- [11] Isara Ar, Osayi N. Knowledge Of Human Papillomavirus And Uptake Of Its Vaccine Among Female Undergraduate Students Of Ambrose Alli University, Ekpoma, Nigeria. *Journal Of Community Medicine And Primary Health Care*. 2021;33(1):64–75.
- [12] Akinfenwa At, Monsur Ta. Burden Of Cervical Cancer In Northern Nigeria. *Tropical Journal Of Obstetrics And Gynaecology*. 2018;35(1):25–9.

- [13] Voss Ds, Wofford Lg. Human Papillomavirus Vaccine Uptake In Adolescent Boys: An Evidence Review. *Worldviews Ev Based Nurs.* 2016 (5):390–5.
- [14] Kumar S, Biswas M, Jose T. Hpv Vaccine: Current Status And Future Directions. *Medical Journal Armed Forces India.* 2015;71(2):171–7.
- [15] Fagbule O, Kanmodi K, Aliemeke E, Ogunniyi K, Ogbeide M, Victor S, Et Al. Knowledge Of Hpv And Hpv Vaccine Among Senior Secondary School Students In Nigeria: Implications Oncancer Prevention Strategies, The Chance Study. *Popul Med.* 2020 Oct 5;1–10.
- [16] Seyoum A, Assefa N, Gure T, Seyoum B, Mulu A, Mihret A. Prevalence And Genotype Distribution Of High-Risk Human Papillomavirus Infection Among Sub-Saharan African Women: A Systematic Review And Meta-Analysis. *Front Public Health.* 2022 10:890880.
- [17] Kombe Kombe Aj, Li B, Zahid A, Mengist Hm, Bounda Ga, Zhou Y, Et Al. Epidemiology And Burden Of Human Papillomavirus And Related Diseases, Molecular Pathogenesis, And Vaccine Evaluation. *Front Public Health.* 2021 8:552028.
- [18] Juckett G, Hartman-Adams H. Human Papillomavirus: Clinical Manifestations And Prevention. *Afp.* 2010 Nov 15;82(10):1209–14.
- [19] Castle Pe, Maza M. Prophylactic Hpv Vaccination: Past, Present, And Future. *Epidemiology And Infection.* 2016;144(3):449–68.
- [20] Bencherit D, Kidar R, Otmani S, Sallam M, Samara K, Barqawi Hj, Et Al. Knowledge And Awareness Of Algerian Students About Cervical Cancer, Hpv And Hpv Vaccines: A Cross-Sectional Study. *Vaccines.* 2022;10(9):1–13.
- [21] Brotherton Jm. Human Papillomavirus Vaccination Update: Nonavalent Vaccine And The Two-Dose Schedule. *Australian Journal Of General Practice.* 2018;47(7):417–21.
- [22] Makwe Cc, Ihuoma R. Human Papillomavirus ( Hpv ) Infection And Vaccines : Knowledge , Attitude And Perception Among Female Students At The University Of Lagos ,. *Journal Of Epidemiology And Global Health.* 2012;2(4):199–206.
- [23] Musa J, Nankat J, Achenbach Cj, Shambe Ih, Taiwo Bo, Mandong B, Et Al. Cervical Cancer Survival In A Resource-Limited Setting-North Central Nigeria. *Infectious Agents And Cancer.* 2016;11(1):1–7.
- [24] Makwe Cc, Anorlu Ri, Odeyemi Ka. Human Papillomavirus (Hpv) Infection And Vaccines: Knowledge, Attitude And Perception Among Female Students At The University Of Lagos, Lagos, Nigeria. *Journal Of Epidemiology And Global Health.* 2012;2(4):199–206.
- [25] Wilson R, Brown Dr, Boothe Mas, Harris Ces. Knowledge And Acceptability Of The Hpv Vaccine Among Ethnically Diverse Black Women. *Journal Of Immigrant And Minority Health.* 2013;15(4):747–57.
- [26] Pitts Mk, Dyson Sj, Rosenthal Da, Garland Sm. Knowledge And Awareness Of Human Papillomavirus (Hpv): Attitudes Towards Hpv Vaccination Among A Representative Sample Of Women In Victoria, Australia. *Sexual Health.* 2007;4(3):177–80.
- [27] Bowyer Hl, Marlow Lav, Hibbitts S, Pollock Kg, Waller J. Knowledge And Awareness Of Hpv And The Hpv Vaccine Among Young Women In The First Routinely Vaccinated Cohort In England. *Vaccine.* 2013;31(7):1051–6.
- [28] Chew Kt, Kampan N, Shafiee Mn. Perception And Knowledge Of Human Papillomavirus (Hpv) Vaccine For Cervical Cancer Prevention Among Fully Vaccinated Female University Students In The Era Of Hpv Vaccination: A Cross-Sectional Study. *Bmj Open.* 2021;11(12):1–7.
- [29] Isara Ar, Osayi N. Knowledge Of Human Papillomavirus And Uptake Of Its Vaccine Among Female Undergraduate Students Of Ambrose Alli University, Ekpoma, Nigeria. *Journal Of Community Medicine And Primary Health Care.* 2021;33(1):64–75.
- [30] Charles I. K. Iwunze, Chukwuma U. Okeafor Bmk. Case Report: Deliberate Self Harm With Multiple Lacerations In A 23 Year Old Depressed Nigerian Male Charles. *Port Harcourt Med J.* 2018;11(3):170–4.
- [31] Elikwu Cj, Ajani Ta, Shonekan O, Nwadike V, Tayo B, Okangba Cc, Et Al. Evaluation Of Awareness Of Human Papillomavirus And Cervical Cancer Among Female Undergraduates Of A Private Mission University In Southwestern Nigeria. *Advances In Microbiology.* 2022;12(11):621–33.
- [32] Attitude Towards Hpv Vaccination And The Intention To Get Vaccinated Among Female University Students In Health Schools In Jordan [Internet]. [Accessed 2024/10/2]. Available From: <https://www.mdpi.com/2076-393x/9/12/1432>
- [33] Constantine Na, Jerman P. Acceptance Of Human Papillomavirus Vaccination Among Californian Parents Of Daughters: A Representative Statewide Analysis. *Journal Of Adolescent Health.* 2007;40(2):108–15.
- [34] Addisu D, Gebeyehu Na, Belachew Yy. Knowledge, Attitude, And Uptake Of Human Papillomavirus Vaccine Among Adolescent Schoolgirls In Ethiopia: A Systematic Review And Meta-Analysis. *Bmc Women’s Health.* 2023;23(1):1–12.
- [35] Ndikom Cm, Oboh Pi. Perception, Acceptance And Uptake Of Human Papillomavirus Vaccine Among Female Adolescents In Selected Secondary Schools In Ibadan, Nigeria. *African Journal Of Biomedical Research.* 2017;20(3):237–44.
- [36] Hopkins Tg, Wood N. Female Human Papillomavirus (Hpv) Vaccination: Global Uptake And The Impact Of Attitudes. *Vaccine.* 2013 Mar 25;31(13):1673–9.
- [37] Ihudiebube-Splendor C, Jisieike-Onuigbo N, Ezeh N, Linda C, Chioma J, Favour C. Attitude And Perceived Barriers To Uptake Of Human Papillomavirus Vaccine Among Female Students In A Nigerian Tertiary Institution. *International Journal Of Medical Research & Health Sciences.* 2019;8(4):85–92.
- [38] Chowdhury S, Chakraborty P Pratim. Universal Health Coverage There Is More To It Than Meets The Eye. *Journal Of Family Medicine And Primary Care.* 2017;6(2):169–70.
- [39] Okunowo Aa, Ugwu Ao, Kuku Jo, Soibi-Harry Ap, Okunowo Bo, Ani-Ugwu Nk, Et Al. Predictors, Barriers And Motivating Factors For Human Papillomavirus Vaccination And Testing As Preventive Measures For Cervical Cancer: A Study Of Urban Women In Lagos, Nigeria. *Preventive Medicine Reports.* 2021;24:101643.
- [40] Ojiji, Dike Ei, Okeudo C, Nzewuihe Ac, Uzoma Mjk. Human Papilloma Virus Vaccine: Awareness And Acceptability Amongst Female Medical Students And Health Workers In A University Teaching Hospital In Eastern Nigeria. *Nigerian Journal Of Surgical Sciences.* 2013;23(1):14.
- [41] Bianco A, Pileggi C, Iozzo F, Nobile Cga, Pavia M. Vaccination Against Human Papilloma Virus Infection In Male Adolescents: Knowledge, Attitudes, And Acceptability Among Parents In Italy. *Human Vaccines & Immunotherapeutics.* 2014;10(9):2536–42.
- [42] Sunday Ao, Dadi H, Yakubu A. Mapping Of The Spatial Distribution Pattern Of Health Care Facilities In Bauchi Metropolis, Using Geographic Information System, Bauchi State, Nigeria. 2022;
- [43] Musa A, Abba U, Abba M, Jibril M, Ibrahim U, Abubakar I, Et Al. Effect Of Health Education Intervention On Knowledge Of Hpv Infection And Vaccine Among Parents Of Adolescent In Kano Metropolis, Nigeria. *European Academic Research.* 2022 ;1x:5237.

- [44] Mohammed A, Okoh E, Osagie I. Uptake Of Human Papiloma Virus Vaccine Among Students Of Tertiary Institutions In Gombe State, Nigeria. *European Journal Of Pharmaceutical And Medical Research*. 2019;6:163–8.
- [45] Knowledge Regarding Cervical Cancer Among Undergraduate Female Students At A Selected College Of Lalitpur, Nepal - Pmc [Internet]. [Accessed 2024/10/2]. Available From: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6970460/>
- [46] Abdullahi Lh. Adolescent Immunisation In Africa In The Decade Of Vaccines. 2019 [Accessed 2024/03/20]; Available From: <https://open.uct.ac.za/handle/11427/30364>
- [47] Bonanni P, Faivre P, Lopalco Pl, Joura Ea, Bergroth T, Varga S, Et Al. The Status Of Human Papillomavirus Vaccination Recommendation, Funding, And Coverage In Who Europe Countries (2018–2019). *Expert Review Of Vaccines*. 2020;19(11):1073–83.
- [48] Maver Pj, Poljak M. Progress In Prophylactic Human Papillomavirus (Hpv) Vaccination In 2016: A Literature Review. *Vaccine*. 2018;36(36):5416–23.
- [49] Bartlett Ja, Peterson Ja. The Uptake Of Human Papillomavirus (Hpv) Vaccine Among Adolescent Females In The United States: A Review Of The Literature. *The Journal Of School Nursing*. 2011;27(6):434–46.
- [50] Dorji T, Nopsopon T, Tamang St, Pongpirul K. Human Papillomavirus Vaccination Uptake In Low-And Middle-Income Countries: A Meta-Analysis. *Eclinicalmedicine* [Internet]. 2021 Apr 1 [Accessed 2024/10/2];34. Available From: [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00116-4/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00116-4/fulltext)