Analysis of database about vaccination against human papillomavirus in Sergipe in 2014

Análise do banco de dados referente à vacinação contra papilomavírus humano no estado de Sergipe no ano de 2014

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ABSTRACT

Introduction: The development of the Human papillomavirus vaccine has created the possibility of action at the primary level for the prevention of cervical cancer and precancerous lesions. **Objective**: To analyze the data obtained by the introduction of the vaccine against papillomavirus in the state of Sergipe, quantifying the sampling population of girls met in 2014 and quantify the hit target by each micro-region of the state. **Methods**: Cross-sectional analysis, descriptive with retrospective component, using only secondary data from the Health State Department - Sergipe, concerning the vaccination coverage of vaccine against human papillomavirus from March 2014 to December 2014 in 11 to 13-year-old girls. Wilcoxon test was used for mean differences in the paired regions, ages and both. **Results**: In the analysis of the study period, a total population of 11 to 13-year-old girls, 61785 received the first dose of the vaccine (D1), reaching a 103.25% coverage and, 30,561 of these received the second dose of vaccine, resulting in a 56.26% coverage. In all analyzed regions decreasing doses applied between the first (D1) and the second dose (D2) were found. In this analysis, the confidence interval to 95% were all small and all data were analyzed statistically significant at $p<0.001$. **Conclusion**: All micro-regions reached the vaccination goal of the State Departament of Health in the application of the first doses and two of them were above the national average. However, none reached the target in the second dose, four micro-regions were below the national average and tree above. The age group of 12 years was the only one to not reach the goal neither in the first nor in the second dose.

Keywords: public health; papillomaviridae; vaccine.

RESUMO

Introdução: O desenvolvimento da vacina contra o Papilomavírus humano criou a possibilidade de agir a nível primário na prevenção de câncer cervical e lesões pré-cancerosas. **Objetivo**: Analisar os dados obtidos através da instituição da vacina contra o Papilomavirus no estado de Sergipe, quantificando amostralmente a população de meninas atendidas no ano de 2014 e quantificar a meta atingida por cada microrregião do estado. **Métodos**: Análise de corte transversal, descritiva, com componente retrospectivo, utilizando-se exclusivamente dados secundários provenientes da Secretaria Estadual de Saúde - Sergipe, referentes à cobertura vacinal contra o papilomavirus humano no ano de 2014 em meninas de 11 a 13 anos de idade. Foi utilizado o teste de Wilcoxon para diferenças de médias pareadas nas regiões, nas idades e em ambos. **Resultados**: No período de análise do estudo, de uma população total de meninas na faixa etária de 11 a 13 anos, 61.785 receberam a primeira dose da vacina (D1), atingindo uma cobertura de 103,25% e destas, 30.561 receberam a segunda dose da vacina gerando uma cobertura de 56,26%. Em todas as regiões analisadas foram encontradas diminuição de doses aplicada entre a primeira (D1) e a segunda dose (D2). Nesta análise, o intervalo de confiança para 95% foram todos pequenos e todos os dados analisados foram estatisticamente significantes com $p<0,001$. **Conclusão**: Todas as microrregiões atingiram a meta de vacinação da Secretaria Estadual de Saúde na aplicação das primeiras doses, duas delas ficaram acima da média nacional. No entanto, nenhuma atingiu a meta na segunda dose, quatro microrregiões ficaram abaixo da média nacional e três acima. A faixa etária de de 12 anos foi a única que não alcançou a meta vacinal nem na primeira, nem na segunda dose.

Palavras-chave: saúde pública; papillomaviridae; vacina.

INTRODUCTION

Cervical cancer has caused thousands of premature deaths in women, especially in those of lower socioeconomic status, being considered the most common sexually transmitted disease (STD) around the world[1].

The discovery of the human papillomavirus (HPV) vaccine has created the possibility of action at primary level for the prevention of cervical cancer and precancerous lesions. The two available HPV vaccines have markedly reduced the incidence of cervical intraepithelial neoplasias, genital warts and cervical cancer throughout the world[2,3].

The Human Papillomavirus (HPV) has more than 100 subtypes and about 20 of these can infect the genital tract. HPV includes a family of DNA viruses that infect basal epithelial cells, causing benign and malignant lesions of the skin and mucosae of the anogenital and upper aero-digestive tract. They are divided into two groups. In the first one are the subtypes that, when associated with other risk factors, are related to the development of intraepithelial neoplasia of the cervix, vulva, penis, vagina and anal area. In the other group are low oncogenic potential subtypes, which are associated with the appearance of benign infections considered as condyloma acuminata[4-6].

Besides cervical cancer, HPV infection is also associated with 90% of anal cancers, over 60% of some types of oropharyngeal cancers and 40% of cancers of the vagina, vulva and penis cancer[7,8].

The recognition of HPV as the primary etiological factor of cervical neoplasia began in the 70s by the German scientist Harald zur Halsen, and this finding was considered one of the most important scientific discoveries, but it was from the 20's that was observed the association of cutaneous warty lesions or mucous membranes with an infectious agent[9].

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Prophylactic HPV vaccines have been developed since 1993, aiming to reduce infection and incidence of cervical cancer. After its approval, a great debate was raised in relation to the risks and benefits of this new way of preventing both the scientific community and the media[10,11].

Three types of vaccine have already been approved: In 2009, the bivalent (HPV 16/18); the quadrivalent (HPV 6/11/16/18) in 2006 and most recently in 2014, in the United States, the ninevalent (HPV 6/11/16/18/31/33/45/52/58), with aproximately 90% of cervical and other HPV-related cancers and precancers potentially being avoided. All are composed by particles similar to the viruses known in English as "like particles viruses" (NPV), which produce copies of the virus' structural protein and are capable of inducing the production of antibodies[12,13].

The Brazilian Ministry of Health adopted, in 2014, the quadrivalent HPV vaccine as a preventive measure, but not therapeutic. The main objective is not the eradication of screening cervical cancer, because the vaccine does not provide protection against all oncogenic HPV subtypes or against other STDs[14]. Initially, the vaccine was applied on teenage girls between 9 and 14 years. However, from January 2017 this scenario changed; the Brazilian Ministry of Health started to offer the vaccine for boys aged between 12 and 13 years, fulfilling the recommendation given by several respected scientific societies such as the Brazilian Societies of Pediatrics, Immunology and Of Obstetrics and Gynecology, among others, in order to protect against penile cancers, throat and anus, also related to HPV[15,16].

OBJECTIVE

To Analyze the data obtained by the introduction of the vaccine against papillomavirus in the state of Sergipe, quantifying the sampling population of girls met in 2014 and to quantify the hit target by each micro-region of the state.

METHODS

This study is a cross-sectional analysis, descriptive with retrospective component, using only secondary data from the Health State Department - Sergipe.

The used data refer to the immunization coverage with the HPV vaccine in the state of Sergipe in the period from March 2014 to December 2014 in 11 to 13-year-old girls. These data were collected in State Management of Vaccine-Preventable Diseases and Immunization of the State Health Departament, through the request of required variables for analysis. Procedures for analysis have been approved by the Research Ethics Committee.

The coverage (dose / population) was stratified by region (Aracaju, Estância, Itabaiana, Lagarto, Nossa Senhora da Glória, Nossa Senhora do Socorro and Propriá), by dose (1 and 2 doses, respectively D1 and D2) and by age (11, 12 and 13 years). Coverage was described by average, confidence interval (95%), stratified by dose, age and both.

Wilcoxon test was used for differences in average pairwise (D1 and D2) in regions, in ages and both. The software used was R Core Team (2015) and the significance level was 5%.

RESULTS

In the analysis of the study period, a total population of 61.785 girls aged 11 to 13 years received the first dose of the vaccine (D1), reaching a 103.25% coverage of the expected target; among these, 30.561 received the second dose of the vaccine against HPV, generating a 56.26% of the expected coverage. When the comparison is made by dividing the areas of the state into seven regions (Aracaju, Lagarto, Estância, Itabaiana, Nossa Senhora da Glória, Nossa senhora do Socorro and Propriá), one realizes that all municipalities have achieved the target for D1, but, when looking at D2, it's noticed that in none the target set for vaccination coverage in statistically significant analysis with $p<0.001$ was achieved (**Table 1**).

Considering all seven regions and the first dose of the vaccine (D1), Nossa Senhora do Socorro was the micro-region that presented the greatest coverage with 115% (95%CI 1.05–1.24). On the second dose (D2), the average coverage of all micro-regions was below the target, being Lagarto the micro-region with the worse average coverage of 56% (95%CI 41–71). Comparing to national data, it was observed that two micro-regions (Estância and Nossa Senhora do Socorro) presented coverage above the national average (108.35%) on first dose (D1), and other regions, despite reaching the target, were below average. On the seond dose (D2), four micro-regions (Aracaju, Estância, Itabaiana e Lagarto) were below the national average (70.68%) and tree of them (Nossa Senhora da Glória, Nossa Senhora do Socorro e Propriá) were above the average, of which Propriá presented greater coverage 76% (95%CI 0.69–0.84); however, as well as the others, it did not reach the target for the second dose (D2).

Through the **Figure 1**, the regions of Aracaju, Estância, Itabaiana, Lagarto, Nossa Senhora da Glória and Nossa Senhora do Socorro had in some places a goal above the expected but failed to raise the average in the region. In the municipalities of Itabaiana and Lagarto region we found Health Centers where the average was much lower than the expected. In the municipalities of the Estância region and Nossa Senhora do Socorro it was observed that in Health Centers the average was well above expectations (**Graphic 1**).

When the variable analyzed is the age range of 11 to 13 years among girls served by the National Program of the Ministry of Health

Table 1 – Average HPV vaccine coverage among girls aged 11 to 13 years, distributed per dose between the municipalities of Sergipe.

	Coverage		p-value
	D1 Average (95%CI)	D2 Average (95%CI)	
Aracaju	1.04 (0.94–1.14)	0.62 (0.46–0.78)	<0.001
Estancia	1.09 (0.98–1.19)	0.65 (0.53–0.77)	<0.001
Itabaiana	1.05 (0.94–1.16)	0.64 (0.49–0.78)	<0.001
Lagarto	1.08 (0.96–1.19)	0.56 (0.41–0.71)	<0.001
Nossa Senhora da Glória	1.00 (0.93–1.07)	0.74 (0.58–0.89)	0.001
Nossa Senhora do Socorro	1.15 (1.05–1.24)	0.73 (0.61–0.84)	<0.001
Propriá	1.00 (0.94–1.07)	0.76 (0.69–0.84)	<0.001

95%CI: confidence interval to 95%; Wilcoxon's test; HPV: human papillomavirus; D1: vaccine's first dose applied; D2: second dose applied.
Source: State Health Secretariat of Sergipe.

Immunization, crossing with the average of the applications of the first and second dose, it is found that the average of the second dose, 0.72 (11 years), 0.59 (12 years) and 0.74 (13 years), are lower than the average of the first dose, with values of p<0.001. The age of 12 was the only one to not reach the goal neither in the first norn in the second dose, with 0.93 and 0.59, respectively (**Table 2**).

For a better visualization of the data, from the construction of Epimaps that demonstrated vaccine coverage in the first and second doses in each municipality where the covers are shown in color (the color red represents those municipalities that were far below the target, the orange municipalities that have reached between 50 and 100% of the target, the lighter green municipalities that have reached between 100 and 150% of the average, and the dark green ones that reached from 150 and 200% of the expected coverage target for the city), it can be noticed the significance of the decline in application rates between D1 and D2 (**Figure 2**).

DISCUSSION

In this study, vaccine coverage against human papillomavirus (HPV) was evaluated in 11 to 13-year-old girls in the state of Sergipe, located in the northeastern region of Brazil. A total of 61.785 girls received the first dose of the vaccine (D1) and of these, 30.561 received the second dose against the human Papillomavirus. Thus, in the application of the first dose after the vaccine's launch in the National Immunization Program of the Ministry of Health, the state of Sergipe reached a coverage of 103.25% compared to the target. However, in the second dose, no region of the state reached the established goal, and the mean state was 56.26%, that is, only about half of the girls who took the first dose returned to their health units to take the second (Source: State Health Secretariat of Sergipe).

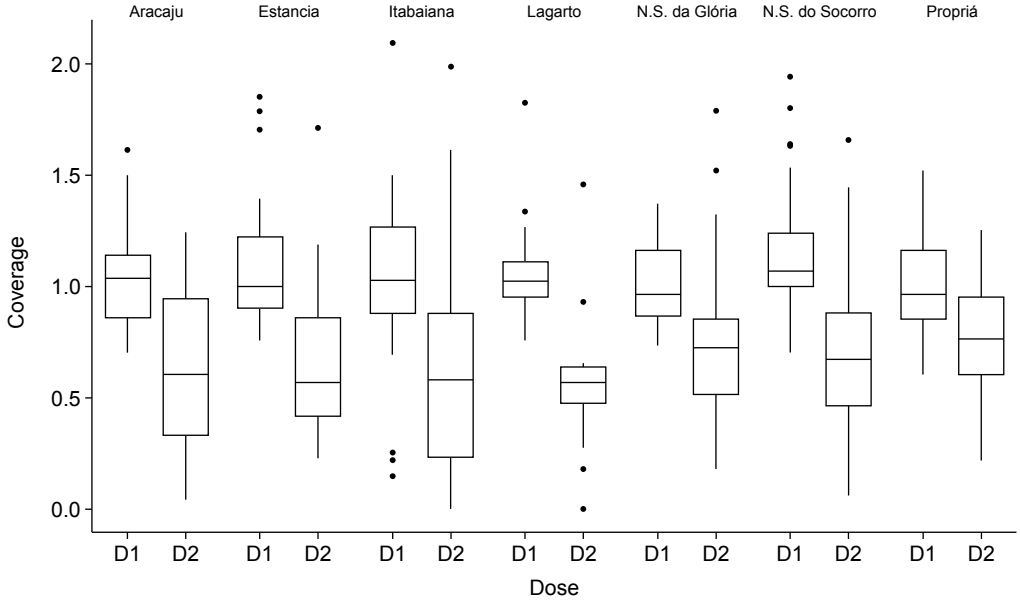
In the region encompassing the state capital, Aracaju, for example, the average coverage of HPV vaccine application in the first dose reached 104% (95%CI 0.94–1.14) and in the second dose the mean was of only 0.62% (95%CI 0.46–0.78) (**Table 1**). When the analysis correlated coverage versus dose by region, the results were not different, and once again showed that there was a decrease in the number of vaccine doses applied at D1 and D2 in all regions. Although some municipalities had a higher total dose applied than their region's average, it was not able to raise the region's average, as the case of Estância and Nossa Senhora do Socorro (**Graphic 1**).

In the analysis of D1 and D2 related to the age of the girls who received the doses, the same result was found and once again a decrease in the number of doses applied in D2. At age 11, the mean D1 was 1.11 and in D2 the mean dose applied was 0.72. At the age of 12, this mean fell from 0.93 to 0.59, and at the age of 13 years, from 1.13 at D1 to 0.74 at D2 (**Table 2**). Graph 2

Table 2 – Average of HPV vaccination coverage among girls aged 11 to 13 distributed by the age group in the state of Sergipe.

Age	Coverage		p-value
	D1 Average (95%CI)	D2 Average (95%CI)	
11	1.11 (1.05–1.17)	0.72 (0.63–0.81)	<0.001
12	0.93 (0.88–0.98)	0.59 (0.52–0.66)	<0.001
13	1.13 (1.07–1.19)	0.74 (0.66–0.83)	<0.001

95%CI: confidence interval to 95%; Wilcoxon's test; HPV: human papillomavirus; D1: vaccine's first dose applied; D2: second dose applied.
Source: State Health Secretariat of Sergipe.



HPV: human papillomavirus; D1: vaccine's first dose applied; D2: second dose of the vaccine.
Source: State Health Secretariat of Sergipe.

Figure 1 – Box Plot of the average HPV vaccine coverage among girls aged 11 to 13 years in the main cities of the state of Sergipe.

also shows the analysis of the relationship between doses one and two in a map of the state of Sergipe, showing the regions that exceeded the target, those that reached and those that were below the target. In this map it is possible to visualize well, through color differentiation, how much of it lost in dose applications from D1 to D2 (**Graph 2**).

This low demand for the second dose may have occurred due to several factors already mentioned in other studies, such as the lack of knowledge about the vaccine, the resistance of parents, especially of the mothers in getting their daughters to receive a vaccine that avoids pathologies related to early sexual life, as well as the negative influence of some communication vehicles, such as when possible side effects were reported after the vaccine was administered to girls in the south of the country[17,18].

In a recent report by Veja magazine, the national incidence of HPV vaccination was low. The magazine released data from the state of São Paulo, where a survey by the State Health Department showed that only 60% of the girls in the target audience would have received the second dose of the vaccine, while in the first dose 100% coverage was achieved. According to the magazine, experts explained that the low numbers could be explained by the following factors: lack of preparation of health professionals and schools participating in the campaign, lack of adequate information about the efficacy and safety of the vaccine for parents and adolescents, the association of HPV with the onset of sexual life and the negative view caused by possible adverse effects suffered by some girls in the coast of the state of São Paulo when receiving the second dose of the vaccine[17, 19]. Most of these facts have been proven in studies, such as Stokley et al.'s[20, 21].

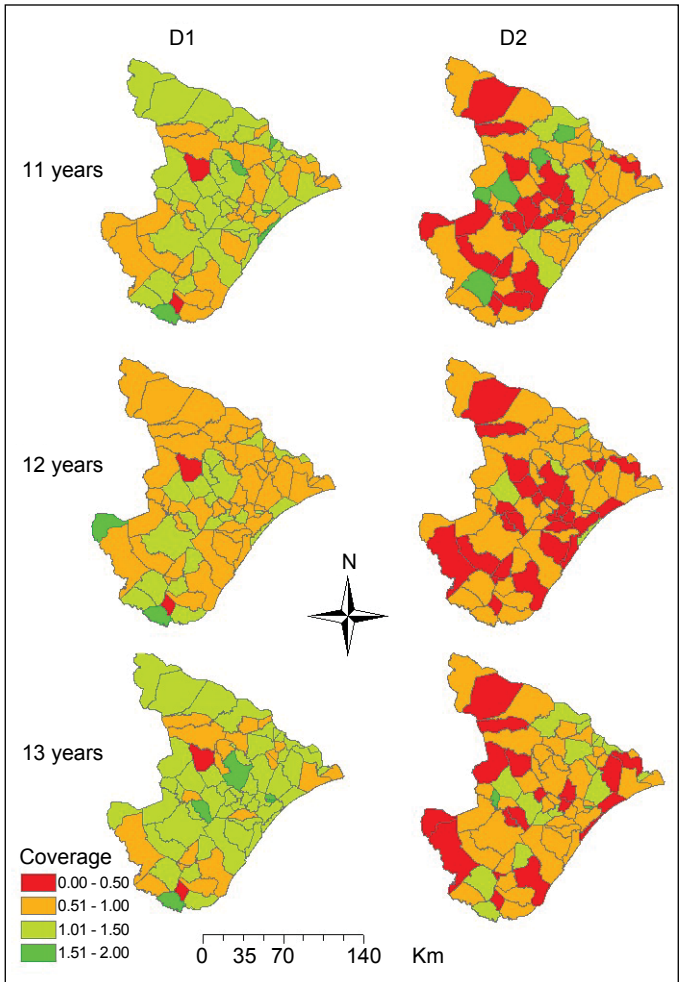


Figure 2 – Map of Vaccine coverage in the state of Sergipe in the year 2014.

Studies have shown that HPV vaccines are an effective way of preventing the pathologies associated with HPV infection[20]. However, despite this evidence and the advertisements made by the Brazilian government and other countries that have adopted the vaccine, recent studies have shown that vaccination rates have not been satisfactory[20,22].

Stokley et al. estimated HPV vaccine coverage between 2007 and 2013 in the United States. Data from this study showed that vaccine doses increased over the years, but coverage remained low in the equivalent period. Among the reasons parents pointed out to not vaccinate their daughters was the lack of knowledge about the vaccine, mainly because they did not find it necessary, due to the possible side effects, because they had not received recommendations or their daughters were not sexually active[20].

In another qualitative study conducted in the United States, Mullins et al. conducted interviews with 11 to 12-year-old girls who received the first dose of the vaccine, their mothers and their doctors. The girls answered questions about HPV and the HPV vaccine, HPV-related risk perceptions and other STIs, sexual behavior, and the influence of mothers, the media, and physicians on perceptions about HPV and vaccine. The mothers answered about the vaccine and about HPV and how it was communicating with their daughters. The doctors answered the knowledge about the vaccine and the attitude towards communicating with the girls and their mothers. Over thirty months, four interviews with the same group occurred, and the study's conclusion was that greater knowledge about HPV vaccines for both mothers and daughters was linked to more accurate perceptions among girls and that the girls' doctors could play an important role in providing education on HPV vaccines for mothers and daughters[23]. Gilkey et al. also analyzed the importance of primary care and the physician's role in discussing with their patients and their mothers, but this would take time to occur and communication strategies about the subject with this audience would still have to be developed. Doctors in this study indicated less HPV vaccine than other vaccines of adolescence[24].

Vaccines against oncogenic types of HPV offer a great potential for primary prevention of the lesions caused by these viruses[25].

Many studies have already enthusiastically pointed out the role of prophylactic vaccines in reducing cervical cancer[26,27]. The prevention of HPV lesions, such as cervical cancers and genital warts, has an impact on the morbidity and mortality associated with these diseases. It has also been shown that both HPV vaccines prevent, in addition to cervical cancer, other types of HPV-related cancers, with moderate to high efficacy[28].

Cervical cancer prevention programs can be effective in reducing the incidence of disease and its mortality when the diagnosis is early, but these measures are difficult to implement in places where resources are scarce. Therefore, HPV vaccines should gain more space because it is estimated that if there is complete vaccination of the population, cases of cervical cancer can be reduced by two-thirds[29]. Since Brazil has already good immunization experiences, it seems to be possible to implement the HPV vaccine as an efficient way to prevent HPV-associated pathologies[30].

Another point to be raised is in relation to the non-viral vaccine, which covers viral types 16/18/31/33/45/52/58 and has already shown in studies a significant increase in the impact on the prevention of HPV lesions in a four-year-old vaccine, which may lead to it being a cost-effective alternative to the quadrivalent vaccine[31].

CONCLUSION

The regions managed to reach the vaccination goal of the State health department in the application of the first doses, but the same did not occur six months after, when the second doses should be given.

The micro-regions of the State of Sergipe reached the vaccination targets at the first dose, which did not happen at the second dose of vaccination.

Girls with age range of 12 years old did not reach the vaccination target in any of the doses.

The micro-region with greater coverage on D1 was Nossa Senhora do Socorro and on D2 was Propriá.

Confiict of interests

The authors declare no conflict of interests.

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