ADVERSE PREGNANCY OUTCOMES (APO) IN 4VHPV VACCINATED ARMENIAN COHORT

Vahe Ter-Minasyan[1,*], Vadim Frolov[2], Gagik Bazikyan[1], Ara Drampyan[1], Vahan Manvelyan[1], Gayane Sahakyan, Hayk Melkumyan
[1]National Institute of Health (Yerevan, Armenia)
[2]"Astghik" Medical Center (Yerevan, Armenia)

Corresponding Author:
e-mail: vaheterm@yahoo.com

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Abstract

Introduction. High coverage of HPV immunization among girls of target age population can significantly increase the efficiency of Cervical cancer (CC) prevention strategy and help the health system to achieve the target prevalence of 4 cases per 100 000 female population, indicated by WHO in 2020. Decreased prevalence of precancerous conditions and cancers verified by screening, finally resulting in decline of CC mortality rates are the most significant proofs of the vaccination importance as a CC primary prevention measure.

We conducted a retrospective, observational cohort study using clinical data for to verify the influence of HPV vaccine (Gardasil, Merck&CO) on pregnancy outcome in women, vaccinated in RA since 2017 year in the limits of anti-HPV vaccination Program (included in National Vaccination Calendar).

Materials and Methods. For the study, we analyzed data contributed by 2 Maternity Hospitals of Yerevan. The clinical data of patients applied to the mentioned Medical Centers within 01.11.2019- 31.10.2023 were retrospectively observed. The data of all 51 women with distal exposure of anti HPV vaccine and all 28 women with pre-pregnancy exposure of anti HPV were engaged in current study. Vaccine exposure windows were considered distal (4vHPV vaccine administered from 22 to 6 weeks before last menstrual period [LMP]) and pre-pregnancy (4vHPV vaccine administered from 42 days before LMP).

The control group was composed by randomly selected women aged 18 to 28 years, who have delivered in one of two mentioned above Maternity Hospitals in the same time frame and have never exposed anti HPV vaccine.

Results. The data obtained regarding the prevalence of complications of anti HPV vaccine exposure shown no significant difference in pregnancy complications' prevalence indicators in patients with the distal and pre-pregnancy exposure of the vaccine. The distal and pre-pregnancy exposure to the quadrivalent anti HPV vaccine was not associated with reliably increased risks of adverse pregnancy outcomes.

Conclusion. The data obtained make us to conclude about non-affected prevalence of adverse pregnancy outcomes in HPV vaccinated cohort in RA. The study results can serve the background for additional confirmation of the safety of the HPV vaccine. The significant elevation of targeted cohort's engagement will, in our opinion, be one of the most important milestones on the path to increasing the HPV control efficacy, while the negative impact on antepartal health indicators are not anticipated.

Keywords: *HPV, vaccination, papillomavirus, adverse pregnancy outcome, safety*

INTRODUCTION

Cervical cancer (CC), in spite of being highly preventable, is the 2nd most common female cancer in women aged 15 to 44 years in Armenia, ranking as the 8th leading cause of female cancer. The age standardized incidence per 100 000 females in Armenia is 7.8, while the age standardized mortality per 100 000 females is 4.6 (115 deaths in 2020 year) [1].

The CC is the 4th most common cancer among women worldwide. Its prevalence was estimated 604,127 new cases and 341,831 deaths in 2020 [2].

CC prevention efficiency may be provided by high coverage of HPV immunization among girls of proper age frame, which is the essential milestone to achieve the target of 4 cases per 100 000 female population, indicated by WHO in 2020 [3,4]. Decreased prevalence

of precancerous conditions and cancers verified by screening, finally resulting in decline of CC mortality rates are the most significant proofs of the importance vaccination as a CC primary prevention measure [5,6].

Among non-vaccinated women, 4-valent vaccine–type HPV detection declined from 32.4% to 19.4% (40% decrease; odds ratio 0.50, 95% confidence interval 0.26 to 0.97). The HPV trends in US community within >10 years post 4-valent HPV vaccine and post 9-valent vaccine period were investigated. The evidence of vaccine effectiveness and herd protection was determined.

However, ambiguous data exist concerning the safety of the quadrivalent HPV vaccine in context of pregnancy outcomes. Some data from different sources published contain the evidences of arguable influence of HPV vaccine exposure in distal or immediate pre-pregnancy period on pregnancy outcome.

The data regarding prevalence of pregnancy course disorders in anti HPV vaccine exposed cohort is not sufficient to judge about its impact on pregnancy and delivery complication.

HPV vaccination (with Gardasil, Merck&CO approved by WHO) was included in the National Immunization Calendar for females aged 13 starting from December 2017 and was then expanded to include females aged 13-45 and males aged 14-45 starting in February 2019. HPV vaccination coverage rates in 2021 and 2022 were 10.8% and 13.3% respectively, and increased to 23.7% for the period from January to April 2023 (girls aged ≤15, last dose) [7].

There is a significant lack of data on vaccination impact on pregnancy and delivery outcome in Armenian population.

All mentioned above stipulated us to undertake the research, aimed to verify the influence of HPV vaccine (Gardasil, Merck&CO) on pregnancy outcome in women, vaccinated in RA since 2017 year in the limits of anti-HPV vaccination program (included in National Vaccination Calendar).

MATERIALS AND METHODS

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in the approval by human research committee. All participants gave written informed consent to participate in the trial and to use their data. The protocol was approved by the Ethics Committee of Named after S.Kh.Avdalbekyan National Institute of Health, RA MOH (Yerevan, Armenia).

The clinical data of patients applied to 2 Medical Centers within 01.11.2019- 31.10.2023 were retrospectively observed. The data of all 51 women with distal exposure of anti HPV vaccine and all 28 women with pre-pregnancy exposure of anti HPV were selected for current study. Vaccine exposure windows were considered distal (4vHPV vaccine administered from 22 to 6 weeks before last menstrual period [LMP]) and pre-pregnancy (4vHPV vaccine administered from 42 days before LMP).

The control group was composed of randomly selected 75 women aged 18 to 28 years, who have delivered in one of two mentioned above Maternity Hospitals in the same time frame and have never been exposed to anti HPV vaccine and any teratogenic factor .

The criteria of inclusion were the following:

1. 16 to 28 years women, whose singleton pregnancies ended between January 1, 2021, and December 15, 2023;
2. who had continuous enrollment from 12 weeks pregnancy through 8 weeks following delivery;
3. who received a 4vHPV vaccine (both doses) in the maximally 6 months period prior to their last menstrual period (LMP).

Exclusion criteria were the following:

1. Spontaneous abortions (SABs) before 6 weeks' gestation,
2. Medical termination of pregnancy before 12 weeks without medical indication,
3. ectopic pregnancies,
4. multiple gestation pregnancies,
5. gestational trophoblastic disease.
6. exposure of teratogenic medication during pregnancy or in the 8 months before pregnancy
7. women with no routine antepartal and postpartal observation.

For pregnancies that were identified as stillbirths, the outcomes were confirmed through medical record review.

The gestational age was based on the early sonogram data, gestational age at delivery or the estimated delivery date.

STATISTICAL DATA PROCESSING

Statistical data processing was performed using the statistical software package SPSS 23 (Statistical Package for Social Science 23) to determine any significant difference in APO prevalence between the groups. For a comparative analysis of the group results (between the HPV vaccinated (distal and pre-pregnancy vaccination) and control groups) obtained after intervention the Kolmogorov-Smirnov test was used revealing the pattern of data distribution, followed by the Student's parametric tests for the comparison of group means. When using the Student test for independent samples, the calculation depended on the statistical significance of differences in the variance of the compared groups.

RESULTS

The Social-demographic Characteristics of the Study Participants

Socio-demographic indicators among the cohort are represented in Table 1. Average age of the study sample was less than 24.2 years old. The dominating marital status was married (61.3%) More than half of the investigated cohort (115 (56.3%)) were multipara, the complications of previous pregnancy were registered in 24 (20.9%) female.

Table 1. The Social-demographic characteristics of the Study Participants' Sample

Characteristic	Total
Age, years	24.2±2.1
Marrital Status	
Married or living together, n (%)	125 (61.3%)
Single, divorced or widowed n (%)	79(38.7%)
Parity	
Primigravida, n (%)	89 (%)
Multipara, n (%)	115 (56.3%)
Complicated previous pregnancy	24 (20.9%)

The data obtained regarding the prevalence of complicatins of anti HPV vaccina exposure are represented in the Table 2. As it is shown in the Table, exposure to the quadrivalent HPV vaccine was not associated with reliably increased risks of adverse pregnancy outcomes.

COMPARISON OF DISTAL EXPOSED WITH NON-EXPOSED PATIENTS

Somatic complications

The Genital-urinary tract diseases prevalence indicators have not demonstrated significant difference (3 cases among 51 distal exposed pregnancies and 5 cases among 75 unexposed pregnancies; prevalence OR = 0.875; 95% CI = [0.199 - 3.835], p = .859).

Maternal infections were diagnosed in 4 case of 51 exposed pregnancies and 6 cases among 75 unexposed pregnancies (prevalence OR= 0.979; 95% CI: [0.262 -3.658], p = .975) in distal exposed and non-exposed pregnancies).

There was no significant difference as well in Venous complications (6 (11.76 %) cases among 51 distal exposed pregnancies vs 9 (12.0%) cases among 75 unexposed pregnancies; OR = 0.978; 95% CI [0.325 - 2.938], p = .966) between distal exposed and non-exposed cohorts).

The Thyroid disorders prevalence indicators as well have not revealed significant difference in distal exposed and non-exposed pregnancies (2 (3.9%) cases among 51 distal exposed pregnancies vs 3 (4%) cases among 75 unexposed pregnancies; OR = 0.979; 95% CI [0.158 - 6.080], p = .982).

The prevalence indicators of Blood Circulation Disorders were not significantly different (2 (2.67%) vs 1 (1.96%) in distal exposure cohort; prevalence OR = 0.73; 95% CI [0.064 - 8.270], p = .799) in exposed and non-exposed patients.

The Anemia prevalence indicators also have not revealed significant difference (18 (35.29%) cases among 51 pre-pregnancy exposed pregnancies and 28 (37.33%) cases among 75 unexposed pregnancies; OR = 0.916; 95% CI [0.437 - 1.921], p = .816).

Obstetrical complications

The indicators of prevalence of Placental Antepartal Haemorrhage And Discoordination Of Uterine Contraction Activity were not as well characterized by reliable difference : 2 (3.9%) case among 51 exposed pregnancies vs 5 (6.66%) cases among 75 unexposed pregnancies; prevalence OR=0.571; 95% CI [0.107 - 3.066], p = .514 - for antepartal placental bleeding and 5 (9.8%) case among 51 exposed pregnancies vs 8 (10.66%) cases among 75 unexposed pregnancies; prevalence OR = 0.91; 95% CI [0.280 - 2.959], p = .876 - for discoordination of uterine contraction activity.

III - IV Degree Perineal Ruptures were revealed in 1 (1.96 %) case among 51 exposed pregnancies and 2(2.67%) cases of 75 unexposed pregnancies (prevalence OR = 0.730; 95% CI [0.644-8.270], p = .799.

Hypertension in Pregnancy (inc. Pregnancy Associated Hypertension, Chronic Hypertension, Severe Pre-Eclampsia and Eclampsia) was diagnosed in 2 (3.9 %) patients in 51 exposed pregnancies and 9 (12 %) women of 75 unexposed pregnancies (prevalence OR= 0.299; 95% CI [0.062 - 1.448], p = .134.

SAB have taken place in 4 (7.8 %) cases of 51 exposed pregnancies and 6 (8.0 %) cases among 75 unexposed pregnancies; prevalence OR = 0.553; 95% CI [0.164-1.872], p = .341.

The difference between indicators of Live Births In Term as well wasn't reliable : 47 (92.16%) case among 51 exposed pregnancies and 69 (92%) cases among 75 unexposed pregnancies; prevalence OR=1.02; 95% CI [0.273- 3.819], p = .974.

Preterm Birth (<37 weeks) and IUGR had the identical distribution in groups. Both were diagnosed in 2 (3.9 %) cases among 51 exposed pregnancies and in 3 (4.0 %) cases of 75 unexposed pregnancies (prevalence OR=0.980; 95% CI [0.158 - 6.080], p = .982.

COMPARISON OF PRE-PREGNANCY EXPOSED WITH NON-EXPOSED PATIENTS.

Somatic disorders

The Genital-urinary tract diseases prevalence indicators have not demonstrated significant difference. The GUTI was revealed in 1 (3.57%) case among 28 pre-pregnancy exposed pregnancies and 5 (6.67%) cases among 75 unexposed pregnancies; OR = 0.519; 95% CI [0.058 - 4.645], p = .557.

Maternal infections was diagnosed in 2 (7.14%) cases of 28 pre-pregnancy exposed pregnancies and in 6 (8.0%) cases among 75 unexposed pregnancies; prevalence OR= 0.885; 95% CI[0.168 - 4.665], p = .884

There was no significant difference as well in Veinous complications: 3 (10.7 %) cases of 28 pre-pregnancy exposed pregnancies and 19 (25.3%) cases among 75 unexposed pregnancies; OR = 0.35; 95% CI[0.096 - 1.305], p = .119) between pre-pregnancy exposed and non-exposed cohorts.

The Thyroid disorders prevalence indicators also have not revealed significant difference: 1 case among 28 pre-pregnancy exposed pregnancies and 3 (4%) cas-

Variable	Non-vaccinated N=75	Distal exposure N=51	Pre-pregnancy exposure N=28	Statistical indicator	Distal exposure vs Non-vaccinated	Pre-pregnancy vs Non-vaccinated
Somatic disorders						
Genital -urinary tract diseases	5 (6.67%)	3 (5.88%)	1 (3.57%)	OR 95%CI p-value	0.875 [0.199 - 3.835] .859	0.519 [0.058 - 4.645] .557
Maternal infections	6 (8.0%)	4 (7.84%)	2 (7.14%)	OR 95%CI p-value	0.979 [0.262 - 3.658] .975	0.885 [0.168 - 4.665] .884
Veinous complications	19 (25.3%)	6 (11.76%)	3 (10.7%)	OR 95%CI p value	0.393 [0.145 - 1.066] .0667	0.354 [0.096 -1.305] .119
Thyroid disorders	3 (4%)	2 (3.9%)	1 (3.57%)	OR 95%CI p-value	0.979 [0.158 - 6.080] .982	0.889 [0.089 - 8.920] .920
Blood circulation disorders	2 (2.67%)	1(1.96%)	---	OR 95%CI p-value	0.730 [0.064 - 8.270] .799	0.516 [0.024 -11.078] .672
Anemia	28 (37.33%)	18 (35.29%)	10 (35.71%)	OR 95%CI p-value	0.916 [0.437 - 1.921] .816	0.933 [0.378 - 2.302] .880
Obstetrical complications						
Placenta previa and placenta abruptio caused antepartal bleeding	5 (6.66%)	2 (3.9%)	1(3.57%)	OR 95%CI p-value	0.571 [0.107 - 3.066] .514	0.519 [0.058 - 4.645] .557
Discoodination of uterine conraction activity	8 (10.66)	5 (9.8%)	3 (10.71)	OR 95%CI p-value	0.910 [0.280 - 2.959] .876	1.005 [0.247 - 4.093] .994
III - IV degree perineal rupture	2 (2.67%)	1 (1.96%)	-----	OR 95%CI p-value	0.730 [0.064 - 8.270] .799	0.516 [0.024 -11.078] .672
Hypertension in Pregnancy (inc. PAH, CHH, severe pre-eclampsia and eclampsia)	9 (12%)	2 (3.9%)	1 (3.57%)	OR 95%CI p-value	0.299 [0.062 - 1.448] .134	0.272 [0.033 2.249] .227
SAB	6 (8.0 %)	4 (7.8%)	2 (7.14%)	OR 95%CI p value	0.979 [0.262 - 3.658] .975	0.885 [0.168 - 4.665] .884
Live births in term	69 (92.0 %)	47 (92.16 %)	26 (92.86%)	OR 95%CI p-value	1.022 [0.273 - 3.819] .974	1.130 [0.214 - 5.961] .885
Preterm birth (<37 weeks):	3 (4.0%)	2 (3.9%)	1 (3.6%)	OR 95%CI p value	0.980 [0.158 - 6.080] .982	0.889 [0.089 - 8.920] .920
SGA/IUGR births	3 (4.0%)	2 (3.90%)	1 (3.60%)	OR 95%CI p-value	0.980 [0.158 - 6.080] .982	0.889 [0.089 - 8.920] .920

es among 75 unexposed pregnancies; OR = 0.89; 95% CI [0.089 - 8.92], p = .920.

Blood circulation disorders were not registered in pre-pregnancy vaccinated patients 0 (0%) and 2 (2.67%) cases were revealed among 75 unexposed pregnancies; (OR= 0.516; 95% CI [0.024 - 11.78], p = .672).

The Anemia prevalence indicators also have not revealed significant difference: 10 (35.7%) cases among 28 pre-pregnancy exposed pregnancies and 28 (37.3%) cases among 75 unexposed pregnancies; OR = 0.933; 95% CI [0.378 - 2.303], p = .880).

Obstetrical complications

Placenta previa and placenta abruptio caused antepartal bleeding was diagnosed in 1 (3.57%) case among 28 pre-pregnancy vaccinated patients and 5 (6.66%) cases of 75 unexposed pregnancies (prevalence OR = 0.52; 95% CI [0.058-4.645], p = .5571).

Discoodination of uterine contraction activity was detected in 3 (10.7%) cases of 28 patients vaccinated in pre-pregnancy period and 8 (10.67 %) cases among 75 unexposed patients; prevalence OR= 1.00; 95% CI [0.25 - 4.09], p = .994.

III - IV degree perineal ruptures were not registered in pre-pregnancy vaccinated patients while 2 (2.67%) cases of III - IV degree perineal ruptures were revealed among 75 unexposed pregnancies; (prevalence OR = 0.516; 95% CI [0.024 - 11.078], p = .672).

Pregnancy Hypertension was diagnosed in 1 (3.57 %) patient of 28 exposed pregnancies and in 9 (12 %) cases among 75 unexposed pregnancies (prevalence OR = 0.272; 95% CI [0.033 - 2.249], p = .227).

SAB has taken place in 2 (7.14 %) cases among 28 with pre-pregnancy exposure of vaccine and 6 (8.0 %) cases among 75 unexposed pregnancies; (prevalence OR = 0.88; 95% CI [0.168 - 4.665], p = .885).

The difference between indicators of live births in term as well wasn't reliable : 26 (92.86%) case among 28 exposed participants and 69 (92.0%) cases among 75 unexposed pregnancies; prevalence OR = 1.130; 95% CI [0.214- 5.961], p = .885.

Preterm birth (<37 weeks) / IUGR were registered in 1 (3.6 %) case among 28 pre-pregnancy exposed patients and in 3 (4.0 %) cases among 75 unexposed pregnancies; prevalence OR=0.889; 95% CI [0.089 - 8.920], p = .920.

DISCUSSION

HPV is a persisting condition that can lead to serious complications inclusive cancer diseases. In published multiple researches with great observational cohorts it was shown that the inadvertent administration of 4vHPV during the peri-conceptional period or during pregnancy was not associated with increased risks of choriamnionitis, PROM, preterm birth, SGA newborns and major structural birth defects. It was also reported that distal or periconceptional 4vHPV exposure was not associated with pregnancy hypertensive disorders [8-11].

The study involving U.S. military women aged 17–28 years who had at least one pregnancy between 2017–2014 showed no relationship between HPV vaccination during pregnancy and adverse outcomes for the mother or the newborn [12].

Wang A, Liu C, Wang Y, et al., performed systematic review for comparison of HPV vaccine exposed pregnancies with the unexposed pregnancies. The RR was calculated. No higher risk for spontaneous abortion (RR, 0.99 [95% CI, 0.90 to 1.08]); stillbirth (RR, 1.16 [95% CI, 0.71 to 1.90]); small for gestational age (RR, 0.96 [95% CI, 0.86 to 1.07]); preterm birth (RR, 1.04 [95% CI, 0.91 to 1.18]); or birth defects (RR, 1.18 [95% CI, 0.97 to 1.43]) or any adverse pregnancy outcomes was revealed [13].

Yan X, Li H, Song B, Huang G, Chang Q,et al. (2023) conducted investigation (systematic review and meta-analysis with trial sequential analysis) of vaccinated and non-vaccinated female cohorts to estimate the risks of adverse pregnancy outcomes, including spontaneous abortion, birth defects, stillbirth, SGA, preterm birth and ectopic pregnancy. No additional risks for HPV vaccine exposures in periconceptional period or during pregnancy was revealed [14].

Scheller NM, Pasternak B, Mølgaard-Nielsen D, et al (2017) investigated a cohort of Denmark female population with registered pregnancy termination between October 1, 2006, and November 30, 2013. National registry content was examined to compare the data on vaccination (with adverse pregnancy outcomes - spontaneous abortion, stillbirth, major birth defect, small size for gestational age, low birth weight, and preterm birth) with the data of non-vaccinated cohort. The propensity score in a 1:4 ratio was matched with non-vaccinated women. The authors came to conclusion that quadrivalent HPV vaccination during pregnancy was not associated with a significantly higher risk of APO comparatively with the non vaccinated cohort [15].

Lipkind H. S. et al. (2017) and Faber MT et al. (2019) as well found no increased risk of spontaneous abortion, stillbirth, or infant mortality following unintended HPV vaccination during pregnancy [16,17].

Our research evidence indicates that Armenian females exposed 4vHPV in their distal (1 year before pregnancy) or pre-pregnancy (8 weeks before pregnancy) periods within limits of National HPV vaccination program didn't demonstrate reliable discrepancy in APO risk incidences compared with the non-exposed participants. The performed comparative statistical analysis of the assessed indicators has revealed the ORs<1 for APOs' indicators. The chance of investigated APOs development in anti HPV vaccine exposed cohort does not exaggerate that in non-exposed sample cohort. The ORs>1 in Live birth in term (1.2544 & 1.1338 correspondingly for pre-pregnancy and distal exposure indicators) are the evidence of comparatively higher probability for Live birth in term in exposed cohort.

The limitation of our study is not-evaluated cohort of probably terminated pregnancy. We were also limited by low number of the study group participants The later limitation is most likely explained by still low coverage of the vaccination program in Armenia.

CONCLUSION

The data obtained make us to conclude about non-affected prevalence of adverse pregnancy outcomes in 4vHPV vaccinated cohort in RA. The study results can serve the background for additional confirmation of the safety of the 4vHPV vaccine. The significant elevation of targeted cohort's engagement will, in our opinion, be one of the most important milestones on the path to increasing the CC control efficacy, while the negative impact on perinatal health indicators is not anticipated.

ՀՂԻՈՒԹՅԱՆ ԱՆԲԱՐԵՆՊԱՍՏ ԵԼՔԵՐԸ ՀԱՅԱՍՏԱՆՈՒՄ 4V-ՄՊՎ-ՈՎ ՊԱՏՎԱՍՏՎԱԾ ԿԱՆԱՆՑ ՄՈՏ

Վահե Տեր-Մինասյան[1,*], Վադիմ Ֆրոլով[2], Գագիկ Բազիկյան[1], Արա Դրամփյան[1], Վահան Մանվելյան[1], Գայանե Սահակյան, Հայկ Մելքումյան

[1]Հայաստանի Հանրապետության Առողջապահության նախարարության Ակադեմիկոս Ս. Ավդալբեկյանի անվան առողջապահության ազգային ինստիտուտ, Երևան, Հայաստան

[2]«Աստղիկ» բժշկական կենտրոն, Երևան, Հայաստան

Ամփոփագիր

Ներածություն. Թիրախային տարիքի աղջիկների շրջանում պատվաստումների բարձր ծածկույթը կարող է զգալիորեն բարելավել արգանդի պարանոցի քաղցկեղի կանխարգելման ռազմավարությունների արդյունավետությունը և օգնել առողջապահական համակարգին հասնել 2020 թվականին ԱՀԿ-ի կողմից նշված՝ 4 դեպք 100,000 կին բնակչության հաշվով թիրախային ցուցանիշին: Սքրինինգի արդյունքներով հաստատված նախաքաղցկեղային վիճակների և քաղցկեղի տարածվածության նվազումը, որն ի վերջո հանգեցնում է արգանդի պարանոցի քաղցկեղից մահացության մակարդակի նվազմանը, պատվաստումների կարևորության ամենակարևոր վկայությունն է որպես արգանդի պարանոցի քաղցկեղի առաջնային կանխարգելման միջոց:

Որպես Պատվաստումների ազգային օրացույցում ներառված ՄՊՎ-ի դեմ պատվաստումների ծրագրի մաս, մենք իրականացրել ենք ռետրոսպեկտիվ կոհորտային հետազոտություն՝ կլինիկական տվյալների կիրառմամբ ՄՊՎ-ի դեմ պատվաստանյութի (Gardasil, Merck&CO) ազդեցությունը Հայաստանի Հանրապետությունում 2017 թվականից ի վեր պատվաստված կանանց հղիության վրա գնահատելու նպատակով :

Նյութեր և մեթոդներ. Վերլուծվել են 2 ծննդատների տրամադրած տվյալները: Ռետրոսպեկտիվ ուսումնասիրվել են նշված բժշկական կենտրոններ այցելած պացիենտների կլինիկական տվյալները 01.11.2019-31.10.2023 ժամանակահատվածում: Ընթացիկ ուսումնասիրության մեջ օգտագործվել են պատվաստանյութի դիստալ (վերջին դաշտանի սկսվելուց 22-ից 6 շաբաթ առաջ) ազդեցությամբ՝ 51 և ամինջապես մինչև հղիությունը (վերջին դաշտանից 42 օր առաջ) ՄՊՎ-ի դեմ պատվաստված 28 կանանց տվյալները: Վերահսկիչ խումբը բաղկացած էր պատահականության սկզբունքով ընտրված 18-ից 28 տարեկան կանանցից, ովքեր ծննդաբերել են նույն ժամանակահատվածում երկու ծննդատներից մեկում, և երբեք չեն ստացել պատվաստում ՄՊՎ-ի դեմ :

Արդյունքներ. Ստացված տվյալները չեն հայտնաբերել հղիության բարդությունների տարածվածության զգալի տարբերություն պատվաստանյութի դիստալ և կամ անմիջական ազդեցության առումով , ինչպես նաև վերջին դաշտանի սկզբից 22-6 շաբաթ առաջ պատվաստաստված հիվանդների մոտ: ՄՊՎ-ի քառավալենտ պատվաստանյութի ազդեցությունը կապված չէ հղիության անբարենպաստ ընթացքի ռիսկի հետ:

Եզրակացություն. Ստացված տվյալները թույլ են տալիս եզրակացնել, որ ՀՀ-ում ՄՊՎ-ի դեմ պատվաստված կոհորտայում հղիության անբարենպաստ ելքերի տարածվածությունը նվազել է, որը կարող է ծառայել որպես վստահելի նախադրյալ ՄՊՎ-ի պատվաստանյութի կիրառման անվտանգությունը հաստատելու համար: Մեր կարծիքով, թիրախային խմբի ներգրավվածության զգալի աճը կդառնա ՄՊՎ-ի դեմ պայքարի արդյունավետության բարձրացման կարևորագույն փուլը՝ առանց պրենատալ առողջության ցուցանիշների վրա բացասական ազդեցության:

Հիմնաբառեր. *HPV, պատվաստում, պապիլոմավիրուս, հղիության անբարենպաստ ելք, անվտանգություն*

НЕБЛАГОПРИЯТНЫЕ ИСХОДЫ БЕРЕМЕННОСТИ (НИБ) У 4в-ВПЧ ВАКЦИНИРОВАННЫХ ЖЕНЩИН АРМЕНИИ

Ваге Тер-Минасян[1,*], Вадим Фролов[2], Гагик Базикян[1], Ара Дрампян[1], Ваан Манвелян[1], Гаяне Саакян, Айк Мелкумян

[1]Национальный институт здравоохранения имени С.Х.Авдалбекяна

[2]Медицинский центр «Астхик», Ереван, Армения

Абстракт

Введение. Высокий охват вакцинацией против ВПЧ среди девочек целевого возраста может значительно повысить эффективность стратегии профилактики рака шейки матки (РШМ) и помочь системе здравоохранения достичь целевого показателя распространенности 4 случая на 100 000 женского населения, указанного ВОЗ в 2020 году. Снижение распространенности предраковых состояний и онкологических заболеваний, подтвержденных результатами скрининга, в конечном итоге приводящее к снижению показателей смертности от РШМ, являются наиболее значимыми доказательствами важности вакцинации как меры первичной профилактики РШМ.

Нами проведено ретроспективное когортное исследование с использованием клинических данных для оценки влияния вакцины против ВПЧ (Гардасил, Merck&CO) на исход беременности у женщин, вакцинированных в РА с 2017 года в рамках Программы вакцинации против ВПЧ (включена в Национальный календарь вакцинации).

Материалы и методы. Проанализированы данные, предоставленные 2 родильными домами .Клинические данные пациенток, обратившихся в указанные медицинские центры в период с 01.11.2019 по 31.10.2023, были ретроспективно изучены. В текущем исследовании были использованы данные всех 51 женщины с дистальным воздействием вакцины против ВПЧ и всех 28 женщин с воздействием вакцины против ВПЧ до беременности. Окна воздействия вакцины считались дистальными если вакцина 4vHPV вводилась в период с 22 по 6 недель до начала последней менструации и до беременности - вакцина 4vHPV вводилась в период с 42 дней до последней менструации. Контрольную группу составили случайно выбранные женщины в возрасте от 18 до 28 лет, которые рожали в одном из двух указанных выше родильных домов в один и тот же период времени и никогда не подвергались вакцинации против ВПЧ.

Результаты. Полученные данные не показали существенной разницы в показателях распространенности осложнений беременности у пациенток с дистальным и воздействием вакцины так же как и с воздействием вакцины за 22-6 недель до начала последней менструации. Воздействие квадривалентной вакцины против ВПЧ не было связано с достоверно повышенными рисками неблагоприятных исходов беременности.

Заключение. Полученные данные позволяют сделать вывод о низмененной распространенности неблагоприятных исходов беременности в когорте вакцинированных против ВПЧ при РА. Результаты исследования могут служить фоном в качестве дополнительного под-

твержденияя безопасности вакцины против ВПЧ. Значительное повышение вовлеченности целевой когорты, по нашему мнению, станет одним из важнейших этапов на пути повышения эффективности контроля ВПЧ, при этом, не ожидается отрицательного влияния на показатели пренатального здоровья.

Ключевые слова: *ВПЧ, вакцинация, папилломавирус, неблагоприятный исход беременности, безопасность*

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