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Reports to the Vaccine Adverse Event Reporting System (VAERS) after Hepatitis A and Hepatitis AB Vaccines in Pregnant women

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Abstract

Objective: To characterize adverse events (AEs) after Hepatitis A vaccines (Hep A) and Hepatitis A and Hepatitis B combination vaccine (Hep AB) in pregnant women reported to the Vaccine Adverse Event Reporting System (VAERS), a spontaneous reporting surveillance system.

Study design: We searched VAERS for AEs reports in pregnant women who received Hep A or Hep AB from 01/01/1996-04/05/2013. Clinicians reviewed all reports and available medical records.

Results: VAERS received 139 reports of AEs in pregnant women; 7 (5.0%) were serious; No maternal or infant deaths were identified. Sixty-five (46.8%) did not describe an AE. For those women whose gestational age was available, most were vaccinated during the first trimester, 50/60 (83.3%) for Hep A and 18/21 (85.7%) for Hep AB. The most common pregnancy-specific outcomes following Hep A or Hep AB vaccinations were spontaneous abortion in 15 (10.8%) reports, elective termination in 10 (7.2%), and pre-term delivery in 7 (5.0%) reports. The most common non-pregnancy specific outcome was urinary tract infection and nausea vomiting with 3 (2.2%) reports each. One case of amelia of the lower extremities was reported in an infant following maternal Hep A immunization.

Conclusions: This review of VAERS reports did not identify any concerning pattern of AEs in pregnant women or their infants following maternal HepA or HepAB immunizations during pregnancy.

Keywords

vaccine safety; surveillance; hepatitis A vaccine; hepatitis A hepatitis B combined vaccine; pregnancy

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Introduction

The first inactivated Hepatitis A vaccines (Hep A) (Havrix®, GSK; Vaqta®, Merck) and Hepatitis A and hepatitis B combination vaccine (Hep AB) (Twinrix®, GSK) were licensed for use in the US in 1995, 1996 and 2001, respectively. [1] Hep A is routinely recommended for young children and is also recommended for certain groups at increased risk for hepatitis A infection, including vaccination during community outbreaks. [1] Hep AB is indicated for vaccination of persons aged ≥18 years against hepatitis A and B. Any person in this age group having an indication for both hepatitis A and B vaccination can be administered Twinrix. [2] The Advisory Committee on Immunization Practices (ACIP) has assessed that no evidence exists to suggest that administration of inactivated vaccines during pregnancy is associated with a risk to the fetus. [3] ACIP recommends that Hep A should be considered for pregnant women at increased risk for this infection; similarly Hep B is recommended for pregnant women who have an indication for Hep B vaccination. [1, 3] Pregnancy is not a contraindication to vaccination with hepatitis B vaccine. Although few studies have assessed the safety of hepatitis B vaccine during pregnancy the limited data available suggests that developing fetuses are not at risk for adverse events (AEs) when hepatitis B vaccine is administered to pregnant women.[4-6]

Currently, there are limited data on the safety of Hep A or Hep AB in pregnancy. Although there is a pregnancy registry maintained by GlaxoSmithKline to collect data on pregnancy and infant outcomes following vaccination with Hep AB, [7] no data has yet been published. To assess the safety of Hep A or Hep AB in pregnant women and their infants exposed during pregnancy, we conducted a review of reports to the Vaccine Adverse Event Reporting System (VAERS) during 1996-2013.

Materials and Methods

Data Sources

VAERS is a spontaneous reporting system co-administered by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA).[8] Established in 1990, VAERS monitors vaccine safety and accepts adverse event (AE) reports following receipt of any US-licensed vaccine [9] VAERS is not designed to assess causal associations between vaccines and AEs; its primary purpose is to detect potential vaccine safety concerns that may warrant further investigations in defined populations.[10] VAERS accepts reports from vaccine manufacturers, healthcare providers, vaccine recipients, and others. Healthcare providers are required to report any AE from the reportable events table [11] and are encouraged to report any AE they consider to be clinical significant, whether or not they believe it was caused by the vaccine. Manufacturers are required to report all AEs of which they become aware. The VAERS report form collects patients' demographic and past medical history as well as details of the AEs and information on vaccinations.[12] It does not specifically collect information on pregnancy status. AE signs and symptoms recorded in each VAERS report are coded by trained staff using an internationally standardized terminology from the Medical Dictionary for Regulatory Activities (MedDRA).[13] Each report can be coded with one or more MedDRA terms. Reports are also classified as serious based on the Code of Federal Regulations [14] if they contain information that the AE resulted

in death, hospitalization, prolongation of hospitalization, life-threatening illness, or resulted in a persistent or significant disability. For this study, we excluded reports on routine hospitalizations for delivery from the "serious" category. Medical records are routinely requested for all serious VAERS reports except those submitted by the vaccine manufacturer. Some reports only describe exposure to vaccine during pregnancy without an AE.

We searched the VAERS database for reports involving pregnant women who had received Hep A or Hep AB in the United States, with or without other vaccines, during January 1, 1996 through April 5, 2013. We conducted an automated search using the following criteria: MedDRA terms in System Organ Classes (SOC) "Pregnancy, Puerperium, and Perinatal Conditions" and "Congenital, Familial and Genetic Disorders", the MedDRA terms "Drug Exposure during Pregnancy" or "Maternal Exposure During Pregnancy", and a text string search for the term "preg" in the report. Reports of pregnant women or their infants exposed in utero that had at least one of these criteria were included in the dataset for further evaluation.

Clinical Reviews

CDC and FDA medical officers reviewed all US reports identified in the VAERS database using the automated search to confirm pregnancy status at time of vaccination, calculate estimated gestational age and characterize AEs. For each report we assigned a primary diagnosis. If more than one AE was reported for the same individual, we assigned the diagnosis based on what we believed was the primary clinical event of concern and assumed the primary event was a pregnancy-specific event unless information suggested otherwise. Complex reports (e.g. major birth defect, pre-eclampsia) were reviewed by physicians on the study team with expertise in obstetrics and neonatology. For purposes of AE description, if a VAERS report described AEs in more than one person (e.g., mother and exposed infant), we treated each person as a separate report. Reports that indicated the reported subject was not pregnant or that Hep A or Hep AB vaccine was administered prior to the last menstrual period were excluded.

Gestational age at the time of vaccination and at the time of the AE was calculated based on the last menstrual period or estimated delivery date found in the VAERS report or medical records. If this information was not provided, we used other information available from the VAERS report or medical record indicative of gestational age (e.g., ultrasound report, reporter's note, hospital records). We used the following definition for trimesters: first (0-13 weeks), second (14-27 weeks), and third (28+ weeks).[15] Spontaneous abortion (SAB) was defined as a fetal demise prior to 20 weeks gestation, stillbirth was defined as fetal demise at or after 20 weeks gestation, and pre-term delivery was defined as a live birth before 37 weeks gestation. Causality between reported AEs and Hep A or Hep AB was not assessed.

Proportional Reporting Ratios

In order to assess for disproportionately higher reporting of AEs after Hep A or Hep AB administered to pregnant women, we calculated proportional reporting ratios (PRRs) [16,17] compared with inactivated influenza vaccines, which have been determined to have an acceptable safety profile in pregnancy.[18,19] We combined Hep A and Hep AB vaccine

reports and compared proportions of MedDRA terms after these vaccines with proportions of the same MedDRA terms after trivalent inactivated influenza vaccines (TIV) and influenza A (H1N1) 2009 monovalent vaccine (MIV) (used during the 2009-10 pandemic) administered without Hep A or Hep AB vaccine to pregnant women. For TIV and MIV administered in pregnancy, we used VAERS reports analyzed in previous studies[18, 19] as well as reports received during 2010-2013. We excluded reports from analysis if no AE was reported or if live vaccines (contraindicated during pregnancy [3]), or anthrax vaccine (not recommended during pregnancy [20]) were administered concomitantly. We identified MedDRA terms with disproportionately higher reporting after Hep A or Hep AB by applying Evans' criteria (PRR ≥ 2.0, Yates-chi-square ≥ 4.0, and number of reports ≥ 3 in reports of HEP A or Hep AB).[16] Clinical reviews were conducted for all MedDRA terms with a PRR ≥ 2.0.

Because VAERS is a routine, government-sponsored surveillance system that does not meet the definition of research, this investigation was not subject to institutional review board review nor informed consent requirements.

Results

During January 1, 1996 through April 5, 2013, VAERS received a total of 21,606 US reports after Hep A or Hep AB vaccination; 134 reports (0.6%) met criteria of pregnancy reports using the automated search and manual review (102 reports after Hep A and 32 after Hep AB). Five reports described maternal and infant AEs in each report, which we treated separately; therefore, there were a total of 139 reports. No maternal or infant deaths were reported.

Characteristics of VAERS reports are presented in Table 1. Sixty-five HepA and HepAB reports (47%) did not describe any AE; 14 (22%) of these reports were submitted because another vaccine not recommended to be administered to pregnant women had been administered (e.g. live attenuated influenza vaccine, quadrivalent human papillomavirus (HPV4), smallpox) (Table 2). In most of the reports where trimester at time of vaccination was known, Hep A (50; 83.3%) or Hep AB (18; 85.7%) vaccines were administered during the first trimester of pregnancy.

The most frequent pregnancy-specific outcome was SAB in 15 (10.8%) reports (Table 2). One stillbirth was reported in a 13 year-old female at 23 weeks gestation which occurred 162 days after vaccination with Hep A, meningococcal and tetanus and diphtheria toxoids vaccine. There were 7 reports of preterm deliveries. Ten elective abortions were reported, none of which described an AE and none indicated the procedure was done as a consequence of vaccination. The most frequent non-pregnancy specific outcomes were urinary tract infection and nausea/vomiting, in 3 (2.2%) reports each (Table 2). One case of immune reconstitution syndrome occurred in a 23 year-old HIV-positive female who received the Hep A vaccine at 16 weeks gestation. The patient was diagnosed with chronic hepatitis B prior to pregnancy. The patient also presented oral herpes simplex 1 lesions. At 36 weeks gestation, the patient delivered a female infant. The infant experienced respiratory syncytial virus and weight loss at an unspecified date after birth.

Twelve reports (8.6 %) indicated adverse infant outcomes. One infant had a major birth defect (absence of both lower extremities), a small patent ductus arteriosus and patent foramen ovale. This infant was born to a 17 year-old mother who received Hep A and HPV4 vaccines concomitantly at approximately 2 weeks gestation. The mother had no reported complications during pregnancy and no exposure to teratogenic drugs was reported. Three of the 7 infants born prematurely had medical problems. One infant born at 35 weeks, presented with an extra digit in the right hand and also had respiratory distress. A second infant, born at 35 weeks was hospitalized at 3 months of age for a supraglottoplasty due to stridor and apnea secondary to laryngotracheomalacia. A third infant was born prematurely at 36 weeks and presented neonatal jaundice and lung immaturity. The outcomes for the other eight infants born are shown in table 2.

Serious reports after Hep A vaccine included: maternal serious reports: stillbirth, premature delivery, polyhydramnios, oligohydramnios and premature labor; infant reports (described above): laryngotracheomalacia, absence of lower limbs, and neonatal jaundice.

Reports after Hep AB

Among 35 reports of Hep AB, 14 (40%) reports did not describe an adverse event, 16 (45.7%) were maternal events, and 5 (14.3%) were infant/neonatal events. Adverse events included: among pregnancy-specific AEs: 3 reports of SAB and elective termination each, 2 reports of premature delivery, and one report each of oligohydramnios, abruption placentae and uterine and abdominal cramps; among non-pregnancy specific AEs: one report each of pelvic pain, sinusitis, nausea and dizziness, paleness, and injection site pain; five reports of infant AEs: 3 reports of jaundice, and one report each of fetal distress, growth under lower lip. Two serious reports after Hep AB included oligohydramnios and neonatal jaundice noted above.

Proportional Reporting Ratios

Higher PRRs were identified for the MedDRA terms ‘Abortion’ and ‘Neonatal disorder’. Six reports contained the code ‘Abortion’ and comprised 3 reports each of spontaneous abortion and elective termination. Two of the spontaneous abortion reports were after Hep A and one after Hep AB. The three elective termination reports were after Hep AB vaccine. One report did not provide information regarding the reason for the procedure. The other two reports of elective termination were scheduled before vaccination for reasons unrelated to vaccination. Three reports after Hep A contained the code ‘Neonatal disorder’ but two referred to the same infant (one report for the mother and the other for her infant). The diagnosis in the two neonatal reports with this code were a report of respiratory syncytial virus infection, and the serious report of laryngotracheomalacia, both described above. No disproportionality was found in reporting of stillbirth, preterm deliveries or the specific MedDRA terms for SAB (in distinction to the overall ‘Abortion’ code described above).

Comment

During the period of this review from 1996 through 2013, 134 pregnancy reports after Hep A or Hep AB were submitted to VAERS. Our review did not find any unusual or unexpected pattern of maternal, infant or fetal AEs. Close to half of reports (47%) did not describe an

adverse event other than the exposure to Hep A or Hep AB during pregnancy. We conducted two levels of analysis to assess the safety of Hep A or Hep AB in pregnancy: clinical review of VAERS reports and available medical records and disproportionality analysis using proportional reporting ratios. The MedDRA codes 'Abortion' and 'Neonatal disorder' were disproportionally reported, however, reports with the code 'Abortion' included both spontaneous abortion and elective termination, and the code for spontaneous abortion alone was not disproportionally reported. Two of the three elective termination reports indicated the procedure was done for reasons unrelated to vaccination. Clinical review of reports did not identify any concerning cluster of maternal or infant AEs following Hep A or Hep AB administration. The most common pregnancy-specific outcome was spontaneous abortion (SAB), observed in 11% of all reports. SAB is a relatively frequent event during pregnancy with rates that vary from 10.4% in women younger than 25 years to 22.4% in women aged 34 years or older. [21] SAB has also been found to be the most common pregnancy-specific outcome in several studies assessing other vaccines administered to pregnant women reported to VAERS. [18, 19, 22]

Although few studies have assessed the safety of Hep A or Hep AB in pregnant women, one study evaluated the risk of SAB in 3,599 pregnant women who inadvertently received either bivalent human papillomavirus vaccine (HPV2) (Cervarix) or Hep A vaccine during pregnancy[23] Investigators reported the risk of SAB was 11.5% of 1,786 pregnant women who received HPV2, compared with 10.2% in a control group of 1,813 pregnant women who received Hep A.[23] In this same study, the rates for stillbirth and premature delivery were 0.8% and 7.5% for HPV2 and 0.7% and 8.5% for Hep A. These findings are reassuring and do not suggest any evidence for an increased risk of SAB, stillbirths, or premature delivery in either group of women when compared to background rates for these conditions. [21,24,25] Among non-pregnancy specific AEs in our review, urinary tract infection and nausea/vomiting were the most common with 3 non-serious reports each. Urinary tract infection is a frequent medical condition which can affect 20% of pregnancies.[26]

One major birth defect was reported, an infant born without both lower limbs. Absence of limb(s) or congenital amelia is a rare birth defect. A multi-center descriptive epidemiologic international study by Bermejo-Sanchez et al [27] found a total prevalence of Amelia (either one or more limbs) to be 1.41 per 100,000 births. In the Bermejo-Sanchez study absence of both lower extremities accounted for approximately 10% of all amelia cases. Amelia has been described in several infants exposed to thalidomide. It is not known what other risk factors and causes may be responsible for this condition. Polydactyly, or presence of an extra digit, presented by one of the infants in this review may be considered a major birth defect if it can be demonstrated that the extra digit is a complete appendage. No medical records were available for this report and the information provided in the VAERS form was very limited therefore we had insufficient information to classify this report as a major birth defect. Both infants received HPV4 concomitantly, and this coupled with lack of denominator data to calculate reporting rates for these conditions, makes it difficult to make any assessment. Major birth defects occur in 3% of live births [28] and we observed no unusual clustering of birth defects in our review.

Any finding in VAERS needs to be interpreted with caution, given its inherent limitations. VAERS is a passive surveillance system that may be prone to biased reporting (over- or underreporting) and inconsistency in the quality and completeness of reports. Because VAERS accepts reports from any reporter, the information provided by individuals with little or no medical training, may adversely affect the quality of the report. Events that occur close to the time of vaccination are more likely to be reported to VAERS. Birth defects may be diagnosed several months after vaccination and may be underreported. VAERS also generally cannot determine whether a vaccine caused an AE.[9, 10] Stimulated reporting can occur following publicity around a potential AE. For example, although the reporting rate for SAB after influenza A (H1N1) 2009 monovalent vaccine reports was below the background rate for SAB in the US pregnant population, it was 25 times higher than the reporting rate to VAERS for SABs after the seasonal influenza vaccine during the period 1990-2009, likely reflecting stimulated reporting.[18, 19] VAERS does not collect data on the number of individuals vaccinated therefore it is not possible to calculate the incidence or prevalence of adverse events.[9]

Conclusion

This review of the VAERS database did not find any concerning pattern of pregnancy specific outcomes among pregnant women or their infants who received Hep A or Hep AB. Although this study is subject to the limitations of spontaneous surveillance systems, it provides valuable information on the safety of this vaccine in pregnancy.

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References

1. Centers for Disease Control and Prevention. Prevention of Hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2006; 55(No. RR-7):1–23
2. Centers for Disease Control and Prevention. Notice to Readers: FDA Approval for a Combined Hepatitis A and B Vaccine. MMWR 2001; 50(No.37); 806–7 [PubMed: 11785573]
3. Kroger AT, Sumaya CV, Pickering LK, Atkinson WL; Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2011; 60:1–60 Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm?s_cid=rr6002a1_e Retrieved 7 19, 2013
4. Ayoola EA, Johnson AO. Hepatitis B vaccine in pregnancy: immunogenicity, safety and transfer of antibodies to infants. Int J Gynaecol Obstet. 1987; 25:297–301. [PubMed: 2887464]
5. Levy M, Koren G. Hepatitis B vaccine in pregnancy: maternal and fetal safety. Am J Perinatol. 1991; 8:227–32. [PubMed: 1827584]
6. Sheffield JS, Hickman A, Tang J, Moss K, Kourosh A, Crawford NM, et al. Efficacy of an accelerated hepatitis B vaccination program during pregnancy. Obstet Gynecol 2011 5; 117(5): 1130–5. [PubMed: 21508752]
7. GlaxoSmithKline Pregnancy Registries. Twinrix® Pregnancy Registry for Twinrix® Hepatitis A & Hepatitis B (Recombinant) Vaccine. Available at: http://pregnancyregistry.gsk.com/twinrix.html Retrieved 7 19, 2013

8. Singleton JA, Lloyd JC, Mootrey GT, Salive ME, Chen RT. An overview of the vaccine adverse event reporting system (VAERS) as a surveillance system. VAERS Working Group. Vaccine. 1999 7 16; 17(22):2908–17. [PubMed: 10438063]
9. Varricchio F, Iskander J, DeStefano F. Understanding vaccine safety information from the Vaccine Adverse Event Reporting System. Pediatr Infect Dis J 2004(23):287–294. [PubMed: 15071280]
10. Chen RT, Rastogi SC, Mullen JR, Hayes SW, Cochi SL, Donlon JA, et al. The Vaccine Adverse Event Reporting System (VAERS). Vaccine. 1994; 12:542–550 [PubMed: 8036829]
11. VAERS Table of Reportable Events Following Vaccination Available at: http://vaers.hhs.gov/resources/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf Retrieved 11 19, 2013
12. Vaccine Adverse Event Reporting System form. Available at: http://vaers.hhs.gov/resources/vaers_form.pdf Retrieved 7 19, 2013
13. Medical dictionary for regulatory activities maintenance and support services organization; 2010 Available at: http://www.meddramsso.com/index.asp Retrieved 7 19, 2013
14. Food and Drug Administration. 21 Code of Federal Regulation Part 600.80. Postmarketing reporting of adverse experiences. 1997; 62: Federal Register: 52252–52253. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=600.80 Retrieved 7 19, 2013
15. Prenatal care. In: Cunningham G, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY, editors. Williams's obstetrics. 23rd edition. New York: McGraw-Hill Companies, Inc.; 2010:189–214.rd
16. Evans SJW, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. Pharmacoepidemiology and Drug Safety. 2001; 10:483–486. [PubMed: 11828828]
17. Banks D, Woo EJ, Burwen DR, Perucci P, Braun MM, Ball R. Comparing data mining methods on the VAERS database. Pharmacoepidemiol Drug Saf. 2005; 14:601–9. [PubMed: 15954077]
18. Moro PL, Broder K, Zheteyeva Y, Walton K, Rohan P, Sutherland A, et al. Adverse events in pregnant women following administration of trivalent inactivated influenza vaccine and live attenuated influenza vaccine in the Vaccine Adverse Event Reporting System, 1990–2009. Am J Obstet Gynecol. 2011; 204:146.e1–7. [PubMed: 20965490]
19. Moro PL, Broder K, Zheteyeva Y, Revzina N, Tepper N, Kissin D, et al. Adverse Events in Pregnant Women Following Administration of Influenza A (H1N1) 2009 Monovalent Vaccine reported to the Vaccine Adverse Event Reporting System (VAERS). Am J Obstet Gynecol. 2011; 205:473.e1–9. [PubMed: 21861964]
20. Wright JG, Quinn CP, Shadomy S, Messonnier N; Centers for Disease Control and Prevention (CDC). Use of anthrax vaccine in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. MMWR Recommit Rep. 2010; 59:1–30.
21. Black S, Eskola J, Siegrist CA, Halsey N, Macdonald N, Law B, et al. Importance of background rates of disease in assessment of vaccine safety during mass immunization with pandemic H1N1 influenza vaccines. Lancet 2009; 374:2115–22. [PubMed: 19880172]
22. Zheteyeva YA, Moro PL, Tepper NK, Rasmussen SA, Barash FE, Revzina NV, et al. Adverse event reports after tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines in pregnant women. Am J Obstet Gynecol 2012; 207:59.e1–7. [PubMed: 22727350]
23. Wacholder S, Chen BE, Wilcox A, Macones G, Gonzalez P, Befano B, et al. Risk of miscarriage with bivalent vaccine against human papillomavirus (HPV) types 16 and 18: pooled analysis of two randomised controlled trials. BMJ. 2010; 340:c712 [PubMed: 20197322]
24. MacDorman MF, Kimeyer SE, Wilson EC. Fetal and perinatal mortality, United States, 2006. Natl Vital Stat Rep 2012; 60(8):1–23. Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr60/nvsr60_08.pdf Retrieved 7 19, 2013
25. Martin JA, Hamilton BE, Ventura SJ, Osterman MJK, Wilson EC, et al. Births: final data for 2010. National Vital Statistics Report. 2012; 61:1–100 Available at: http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_01.pdf Retrieved 8 9, 2013
26. Vazquez JC, Abalos E Treatments for symptomatic urinary tract infections during pregnancy. Cochrane Database Syst Rev. 2011 1 19 ;(1):CD002256 [PubMed: 21249652]
27. Bermejo-Sánchez E, Cuevas L, Amar E, Bakker MK, Bianca S, Bianchi F, et al. Amelia: a multi-center descriptive epidemiologic study in a large dataset from the International Clearinghouse for

Birth Defects Surveillance and Research, and overview of the literature. Am J Med Genet C Semin Med Genet. 2011; 157C:288–304 [PubMed: 22002956]

28. Correa A, Cragan JD, Kucik JE, Alverson CJ, Gilboa SM, Balakrishnan R, et al. Reporting birth defects surveillance data 1968-2003. Birth Defects Res A Clin Mol Teratol. 2007; 79:65–186. [PubMed: 17278144]

Condensation of the paper:

Review of the VAERS database did not find any concerning pattern of adverse events among pregnant women who received Hepatitis A or Hepatitis AB vaccine

Table 1.

Characteristics of the Vaccine Adverse Event Reporting System (VAERS) reports received following hepatitis A (Hep A) or combination hepatitis A and hepatitis B (Hep AB) vaccines in pregnant women and their infants, United States, January 1, 1996-April 5, 2013 (N=134)

Characteristic	Hep A (N=102)	Hep AB (N=32)
Serious reports, n (%)	5 (4.9)	2 (6.3)
Maternal age in years, median (range) [a]	17 (13-38)	28 (19-39)
Gestational age in weeks at time of vaccination, median (range) [b]	4.0 (0.4-34)	5.7 (2.7-35)
Trimester of pregnancy at time of vaccination [b], n (%)	**N=60**	**N=21**
First (0 – 13 weeks)	50 (83.3)	18 (85.7)
Second (14 – 27 weeks)	8 (13.3)	1 (4.8)
Third (28 + weeks)	2 (3.3)	2 (9.5)
Brand name of vaccine, (n=134), n (%)		
Havrix ®	55 (53.9)	NA
Vaqta®	30 (29.4)	NA
Twinrix®	NA	31 (96.9)
Unknown	17 (16.7)	1 (3.1)
No. reports given with other vaccines [c], n (%)	91 (89.2)	20 (62.5)
No. reports given with at least one live vaccine, n (%)	57 (55.9)	12 (37.5)
Type of reporter, n (%)	**N=102**	**N=32**
Manufacturer	44 (43.1)	17 (53.1)
Provider	35 (34.3)	9 (28.1)
Other [d]	22 (21.6)	5 (15.6)
Patient/parent	1 (1.0)	1 (3.1)

[a] Maternal age was missing in 3 reports after Hep A and Hep AB, each

[b] Gestational age and trimester at time of vaccination was unknown for 52 Hep A and 11 Hep AB reports, respectively

[c] Most common vaccine combination Hep A and Quadrivalent Human Papillomavirus Vaccine (HPV4) in 16 (11.9%) reports

[d] May include office secretary,

Table 2.

Reported adverse events [a] in pregnant women and their infants following receipt of hepatitis A (Hep A) or combination hepatitis A and hepatitis B (Hep AB) vaccines, Vaccine Adverse Event Reporting System (VAERS), January 1, 1996-April 5, 2013 (N=139)

Adverse Events	N	%
Pregnancy-specific AEs		
Spontaneous abortion	15	10.8
Elective termination	10	7.2
Preterm delivery [b]	7	5.0
Preeclampsia	2	1.4
Vaginal bleeding	2	1.4
Oligohydramnios	1	0.7
Polyhydramnios	1	0.7
Stillbirth	1	0.7
Abruption placentae	1	0.7
Failure to progress during labor	1	0.7
Total	41	29.4
Non-pregnancy specific outcomes		
Urinary tract infection	3	2.2
Nausea with/without vomiting	3	2.2
Non-anaphylaxis allergic reactions	2	1.4
Pain in extremity	2	1.4
Other [c]	11	7.9
Total	21	15.1
Infant/neonatal outcomes		
Absence of lower extremities	1	0.7
Extra digit in right hand, respiratory distress	1	0.7
Neonatal jaundice	3	2.2
Supraglottoplasty in infant with laryngotracheomalacia	1	0.7
Large for gestational age	1	0.7
Pneumonitis, respiratory syncytial virus, jaundice	1	0.7
Respiratory syncytial virus, weight loss	1	0.7
Grunting, crying and flatulence	1	0.7
Fetal distress	1	0.7
Growth under lower lip	1	0.7
Total	12	8.6
No Adverse Event Reported	65	46.8

[a] Adverse events are based on primary reported diagnosis identified during clinical review. Maternal and infant outcomes in 4 reports were treated as separate reports

[b] The pregnant woman in one serious report of preterm delivery at 36 weeks gestation also presented with immune reconstitution syndrome and oral herpes simplex;

[c]Other non-pregnancy specific outcomes included one report each of hypoesthesia, injured arm, abdominal pain, dry mouth, syncope, pelvic pain, sinusitis, uterine and abdominal cramps, pallor, non-responsiveness, injection site pain, and lower back pain