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- Clinical Secretary Mumbai Ob Gyn Society
- Assistant Secretary Journal of Obstetrics & Gynecology of India
- Co Editor Journal of Postgraduate Gynecology and Obstetrics
- Fields of interest: High risk obstetrics, adolescent health & contraception, urogynecology

Vaccination of pregnant women

(To protect the mother and infant)

Goals of this Discussion

- Impact of influenza on pregnancy
- Influenza vaccine in pregnancy
- Efficacy and safety of vaccine in pregnancy
- Challenges in vaccinating pregnant women
- Conclusions and key messages

Impact of influenza on pregnancy

Influenza immunology in pregnancy

Epidemiology in pregnancy and infancy

Effect of influenza on mother and fetus

Physiology of infection in the pregnant woman

- Pregnancy does not increase susceptibility to influenza infection, but pregnant women are more likely to experience serious complications and death
- Pregnancy is characterized by marked changes in physiology of many organ systems (fluid balance, lung volume) that impact respiratory physiology
- A combination of pregnancy-specific immune alterations and anatomic and physiological alterations increases the risk of serious complications

Influenza in pregnancy

- Influenza is more likely to cause severe illness in pregnant women than in women who are not pregnant
- Women in the 2nd and 3rd trimesters of pregnancy are at increased risk for hospitalization, severe illness and even death from influenza

Global epidemiology

- In 2009 influenza pandemic:
- Pregnant women accounted for 6% of influenza related hospitalizations, ICU admissions, and deaths
- In the 18–29 years age group, pregnancy accounted for up to 29% of influenza-associated hospitalizations and 16% of deaths

Acta Obstetricia et Gynecologica Scandinavica. Volume 94, Issue 8, pages 797–819, August 2015

Epidemiology – Indian data

Author	Region	Prevalence	Mortality
Mathur et al. (2013)	Jodhpur (West India)	Influenza A (pH1N1):23.4%	Maternal mortality: 70% Mortality in third trimester: 80%
Mehta et al. (2013)	Kochi, Kerala South India)	Influenza A (H1N1): 5.2%	Maternal mortality: 33% Loss of fetus: 33% Preterm delivery: 33%
Gunasekaran (2012)	Chennai (South India)	Influenza (pH1N1):21.4% Influenza A/H3: 9.5% Influenza B: 1.6%	
Pramanick et al. (2011)	Vellore (South India)	ILI/SARI – 29%	Maternal mortality: 25% Fetal mortality: 1
Koul et al., 2016	Kashmir Valley (North)	Influenza - 18.8% • A/H1N1pdm09 - 86% of influenza infection • A/H3n2- 12% • B virus – 2%	Mortality – 8%

Hindawi Publishing Corporation. Infectious Diseases in Obstetrics and Gynecology. Volume 2015, Article ID 867587, 8 pages

Outcome in pregnancy

- Primary viral influenza pneumonia
- Hospitalization
- Adverse pregnancy and birth outcomes
- Morbidity and mortality

Inter-pandemic period: 18-fold higher risk of hospitalization compared to healthy non-pregnant women

Infectious Diseases in Obstetrics and Gynecology Volume 2015, Article ID 867587

Impact on mother

Hospitalization and ICU admissions

Cox et al., 2006

Hospitalizations during pregnancy due to respiratory illness: 1998-2002

- Higher admissions among pregnant women during influenza season (3.4 /1000 vs.1.8/1000 off season)
- Pregnant women with comorbid conditions were 3 times more likely to be hospitalized

Dodds et al., 2007

Hospitalizations during pregnancy compared to before pregnancy: 1990–2002

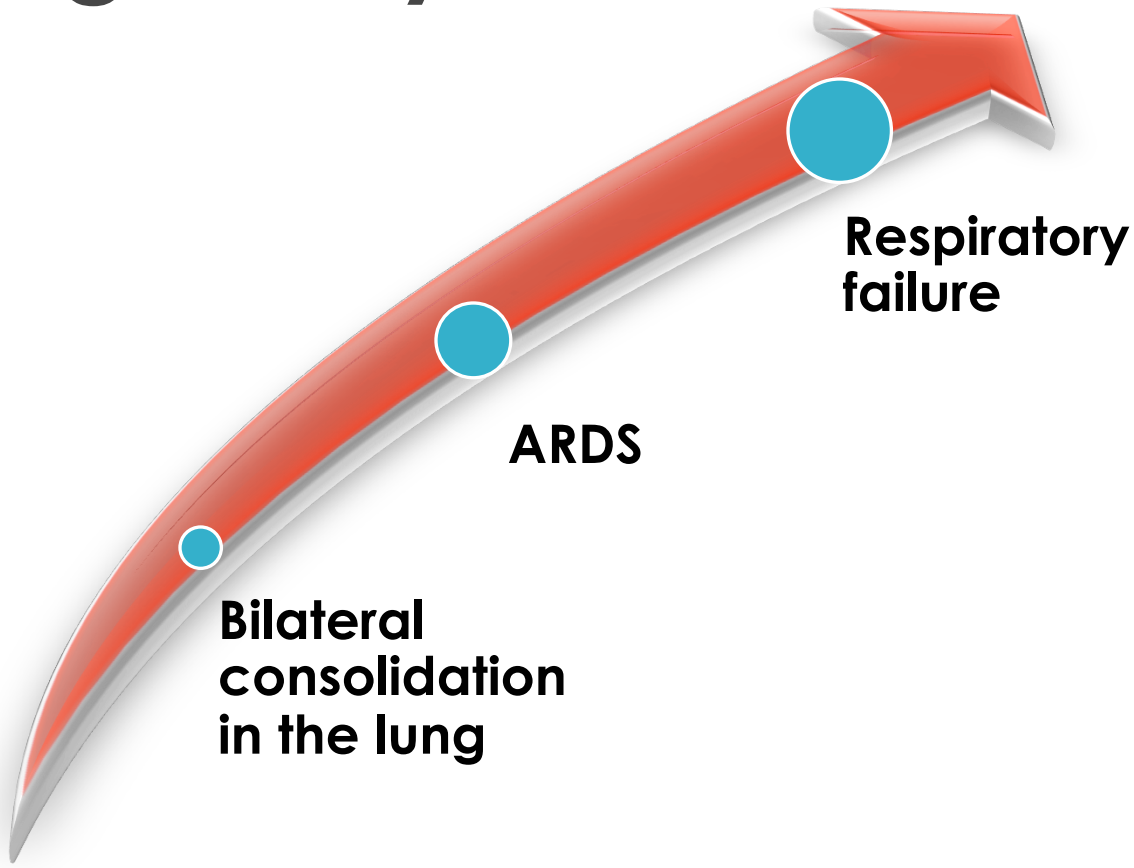
- Likelihood of hospitalization for respiratory complications during influenza season: 1.7 in 1st, 2.1 in 2nd and 5.1 in 3rd trimesters

Mosby et al., 2001

USA, Australia: Pregnant population 1%, but 6.3% of hospitalizations, 5.9% of ICU admissions, 5.7% of deaths

Cox S, et al. Hospitalizations with respiratory illness among pregnant women during influenza season. Obstet Gynecol 2006;107:1315-22., Dodds L, et al. Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. CMAJ 2007;176:463-8., Mosby LG et al. 2009 pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature. Am J Obstet Gynecol. 2011 Jul;205(1):10-8.

Common causes of death in pregnancy



Journal of Evidence Based Medicine and Healthcare 2014; 1:1106-1114

Impact on fetus

Preterm delivery, LBW, SGA, stillbirth, infant death

McNeil et al., 2012

- Babies born to mothers hospitalized for influenza during pregnancy were more likely to be born small for gestational age and to have lower mean birth weight

Pierce et al., 2011

- H1N1 during pregnancy significantly increased perinatal mortality (39/1000 vs. 7/1000) primarily due to still births

US CDC study

Women who delivered while hospitalized for 2009 H1N1 illness, 63.6% were born pre-term, 43.8% delivered low birth weight infants, 69.4% admitted to NICU and 29.2% had 5 min Apgar scores≤6

Background Paper on Influenza Vaccines and Immunization. SAGE Working Group: April 2012, McNeil SA, et al. Effect of respiratory hospitalization during pregnancy on infant outcomes. Am J Obstet Gynecol 2011;204(suppl):S54-7., Pierce M, et al. Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. BMJ 2011;342:d3214., stacks.cdc.gov/view/cdc/29047cdc_29047_DS1.pdf

Impact on fetal outcome

- Indian studies have reported high fetal mortality and prematurity rates

Fetal mortality	Incidence of prematurity
5.5-33 %	20-33 %

International Journal of Gynecology and Obstetrics 2011; 113;1: 32–35
JAPI 2011;59;1:14–18
Journal of Clinical and Diagnostic Research 2013;7;10:2227–2230

Influenza vaccine in pregnancy

Recommendations

General Guidelines

- As a rule, live viral vaccines are contraindicated; inactive are safe
- But the risk is largely theoretical
- Women who have inadvertently received live vaccine during pregnancy should not be counseled to terminate the pregnancy for teratogenic risk
- Non pregnant women should delay pregnancy for 4 weeks

ACIP December 2012

General guidelines

- Benefits of vaccinating pregnant women usually outweigh potential risks when
  - the likelihood of disease exposure is high
  - when infection would pose a risk to the mother or fetus
  - when the vaccine is unlikely to cause harm

2012, 87, 461–476 No. 47

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

23 NOVEMBER 2012, 87th YEAR / 23 NOVEMBRE 2012, 87e ANNÉE
No. 47, 2012, 87, 461–476
http://www.who.int/wer

Contents

Vaccines against influenza WHO position paper – November 2012

Note de synthèse de l'OMS concernant les vaccins antigrippaux – novembre 2012

- **Pregnant women – highest priority group – vaccination in any trimester**
- Healthcare workers
- Children 6 to 59 months of age
- The elderly
- Those with high-risk conditions

Benefits of vaccination *Mother*

- Immunization generates a robust immune response in pregnant women, similar to non-pregnant healthy adults
- Effective protection from the 3 vaccine strains (possible cross-protection against related strains)
- Prevention of influenza complications
- Decreased need for hospitalization for severe disease
- Decrease in adverse pregnancy & perinatal outcomes

Background Paper on Influenza Vaccines and Immunization. SAGE Working Group: April 2012

Benefits of vaccination

Fetus and Neonate

- Decreased proportion of preterm births, LBW, SGA
- Transplacental transfer of antibodies to fetus, providing some protection
- Decreased lab confirmed influenza in neonates

Background Paper on Influenza Vaccines and Immunization. SAGE Working Group: April 2012

ACOG recommendation

The American College of Obstetricians and Gynecologists
Women's Health Care Physicians

COMMITTEE OPINION

Number 468, October 2010 (Replaces No. 305, November 2004)

Committee on Obstetric Practice

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

"Preventing influenza during pregnancy is an essential element of prenatal care, and the most effective strategy for preventing influenza is annual immunization"

ACOG recommendation

- Influenza vaccination is an essential element of preconception, prenatal, and postpartum care because pregnant women are at an increased risk of serious illness due to seasonal and pandemic influenza
- It is critically important that all obstetrician–gynecologists advocate and provide the influenza vaccine to their pregnant patients every season

CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

For influenza, prevention is the only effective intervention

ACIP and CDC recommendations

- Women in the second and third trimesters of pregnancy are at increased risk for hospitalization from influenza. Because vaccinating against influenza before the season begins is critical, and because predicting exactly when the season will begin is impossible, routine influenza vaccination is recommended for all women who are or will be pregnant (in any trimester) during influenza season
- LAIV is contraindicated in pregnancy

International recommendations

- Recommendations across the world (RCOG, SOGC, RANZCOG, AAP) confirm that prevention of influenza by administration of inactivated influenza vaccine is the best intervention in pregnancy
- Vaccination should be given in any trimester or prior to pregnancy planning
- If the woman develops influenza, then Oseltamivir is the drug of choice

Indian Guidelines

- FOGSI recommendations 2014
- Association of Physicians of India 2012
- Ministry of Health and Family Welfare, October 2015
  - "Vaccine helps protect women and their babies up to 6 months and among the vaccinated, there is reduction in influenza related hospitalizations across all ages
  - Vaccine is recommended irrespective of the duration of pregnancy"

Effectiveness of influenza vaccine

Clinical efficacy in mother

Transfer of antibodies

Clinical efficacy in newborn

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effectiveness of Maternal Influenza Immunization in Mothers and Infants

K. Zaman, M.B., B.S., Ph.D., Eliza Roy, M.B., B.S., D.C.H., Shams E. Arifeen, M.B., B.S., Dr.P.H., Mahbubur Rahman, M.B., B.S., Ph.D., Rubhana Raqib, Ph.D., Emily Wilson, M.H.S., Saad B. Omer, M.B., B.S., Ph.D., Nigar S. Shahid, M.B., B.S., M.P.H., Robert F. Breiman, M.D., and Mark C. Steinhoff, M.D.

Mother's Gift Trial, Bangladesh

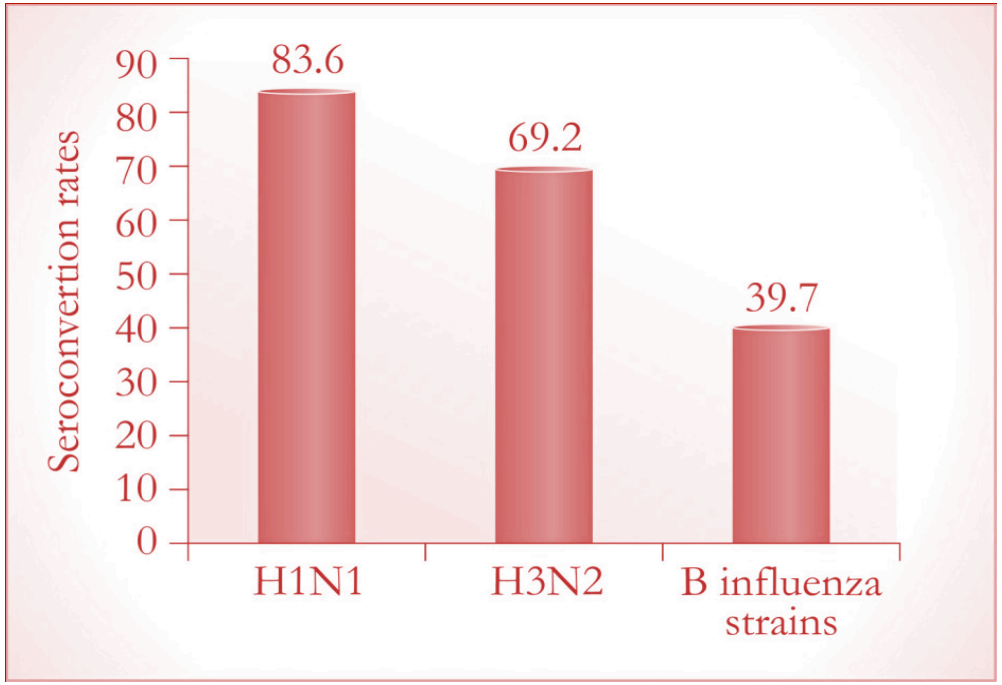
Mother's Gift Trial

- Randomized, blinded trial of 340 mothers in the 3rd trimester
- Maternal TIV decreased respiratory illness with fever
  - 29% among infants; 36% among their mothers
- Reduced proven influenza illness by 63% in infants up to 6 months of age

Zaman, K., et al., Effectiveness of maternal influenza immunization in mothers and infants. The New England journal of medicine, 2008. 359(15): 1555-64.

Immunogenicity studies

Pregnant women had significant increase in their GMTs to the H1N1, H3N2 and influenza B strains following vaccination and seroconversion rates, which are similar to those seen among healthy adults receiving seasonal influenza vaccination



Steinhoff MC, et al. Influenza immunization in pregnancy—antibody responses in mothers and infants. N Engl J Med 2010;362:1644-6.

Immunogenicity studies

Demonstrated protective titers of antibodies in both mother and infants up to age of 6 months

Virus subtype and vaccine group	Mothers		Infants		
	Before immunization	At delivery	At birth	At 10 wk	At 20-26 wk
	Geometric mean titer (95% CI)				
A/New Caledonia (H1N1)					
Controls	12.1 (10.5-14.0)	12.0 (10.5-13.7)	8.0 (7.0-9.1)	5.3 (5.1-5.6)	5.2 (5.0-5.4)
Vaccines	**9.6 (8.3-11.2)**	**166.0 (130.0-212.1)**	**180.2 (139.9-232.0)**	**41.7 (32.5-53.7)**	**11.5 (9.8-13.5)**
A/Fujian (H3N2)					
Controls	51.1 (40.8-63.9)	46.3 (37.6-57.0)	87.3 (72.4-105.2)	26.8 (22.6-31.7)	12.9(10.9-15.3)
Vaccines	**75.7(60.5-94.8)**	**392.2 (332.2-462.8)**	**381.5 (330.5-440.2)**	**105.7 (89.8-124.3)**	**27.6 23.2-32.9)**
B/Hong Kong					
Controls	7.2(6.5-8.0)	7.1 (6.4-7.8)	5.4 (5.2-5.7)	5.0 (5.0-5.0)	5.1(5.0-5.2)
Vaccines	**7.6(6.8-8.5)**	**26.0 (21.3-31.8)**	**22.7 (18.4-28.0)**	**8.4 (7.4-9.6)**	**5.3 (5.1-5.5)**

Transfer of antibodies to fetus

Tsatsaris et al., 2009

HI after maternal IIV vaccination in pregnancy

Infant titers of ≥ 1:40 were observed in 95% of the 88 cord-blood samples tested, and cord-blood titers were significantly higher than maternal blood titers. Neither gestational age at vaccination nor delivery significantly affected the neonatal seroprotection rates

Jackson et al., 2011

HAI titers of ≥1:40 were found in 87% of samples from the 25 μg dose group and in 89% from the 49 μg dose group

The transfer of antibodies from mother to fetus results in robust HI titers in the fetus irrespective of the gestational age at which the mother is vaccinated

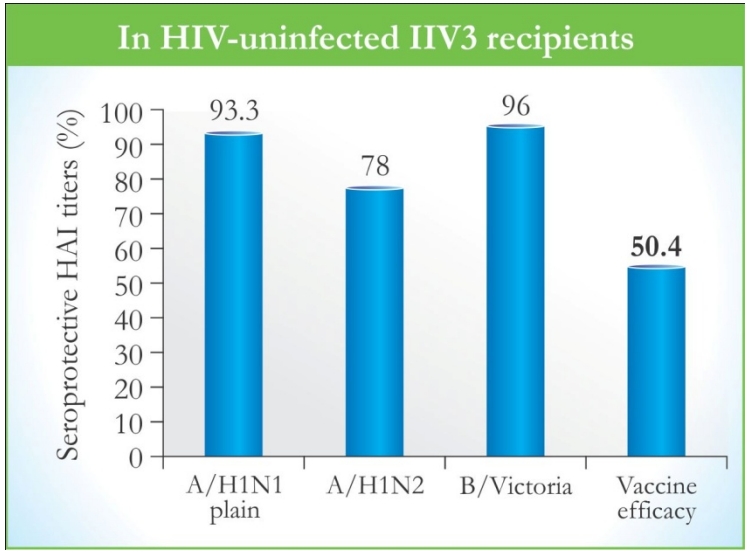
Clinical efficacy in mother

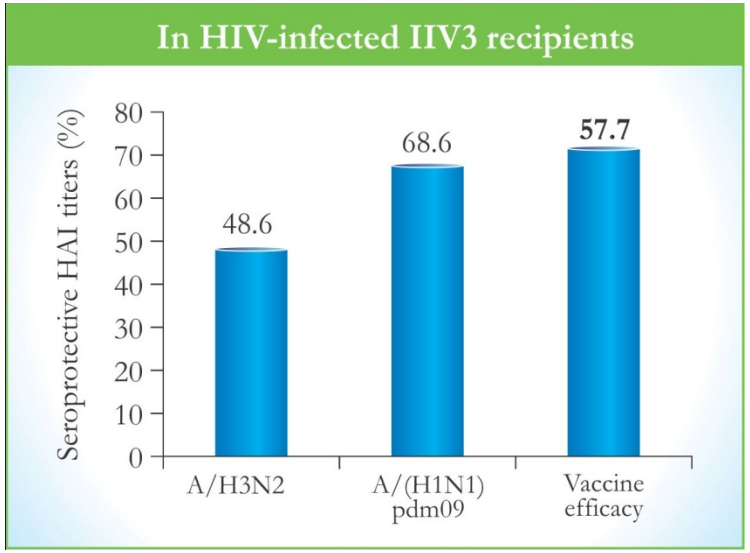
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Influenza Vaccination of Pregnant Women and Protection of Their Infants

Shabir A. Madhi, M.D., Ph.D., Clare L. Cutland, M.D., Locadiah Kuwanda, M.Sc., Adriana Weinberg, M.D., Andrea Hugo, M.D., Stephanie Jones, M.D.,





- Vaccine-efficacy rate 50.4% in HIV-uninfected; 57.7% in HIV-infected
- Influenza vaccine was immunogenic in HIV-uninfected and HIV-infected pregnant women and provided protection against confirmed influenza in both groups of women and in infants who were not exposed to HIV

Clinical efficacy in newborn

Influenza Vaccine Given to Pregnant Women Reduces Hospitalization Due to Influenza in Their Infants

Isaac Benowitz,[1] Daina B. Esposito,[1] Kristina D. Gracey,[1] Eugene D. Shapiro,[1,2,3] and Marietta Vázquez[1]
Departments of [1]Pediatrics and [2]Investigative Medicine, and [3]Public Health, Yale University School of Medicine, New Haven, Connecticut

Measure	Subjects aged <6 months	Subjects aged ≥6 months
No. (%) of case infants; no. (%) of control infants		
Mother was vaccinated	2 (2.2); 31 (19.9)	1 (4.6); 2 (5.6)
Mother was not vaccinated	89 (97.8); 125 (80.1)	21 (95.5); 34 (94.4)
Vaccine effectiveness (95% CI), %		
Unadjusted	90.7 (59.9–97.8)	41.4 (2257.3 to 91.5)
Adjusted	91.5 (61.7–98.1)	

Adjusted vaccine efficacy was 91.5% in infants <6 months of age

Clinical Infectious Diseases 2010; 51(12):1355–1361

Effectiveness of influenza vaccine

- Pregnant women had significant increase in GMTs to the H1N1, H3N2 and influenza B strains following vaccination and seroconversion rates
- Maternal influenza vaccine decreased respiratory illness with fever in infants and mothers
- The immunogenic response to the Inactivated Influenza vaccine is unaffected by and is equivalent to that in the non-pregnant state

Fetal Risk Averted by Maternal Immunization

Study	Site/ Design	Case	Comparison	Results
Steinhoff CJAM 2012 (Mother's Gift)	Bangladesh 2004-05 / RCT	Maternal influenza immunization (172)	No maternal influenza immunization (168)	Newborns exposed to vaccine were 200 gm larger, 34% less likely to be **small for gestational age**
Omer PLoS Med 2011	USA 2004-06 / Retrospect. Cohort	Maternal influenza immunization (578)	No maternal influenza immunization (3,748)	Newborns exposed to vaccine had 70% less **small for gestational age**
Fell AJPH 2012	Canada 2009-10 / Retrospect. Cohort	Maternal influenza immunization (23,340)	No maternal influenza immunization (32,230)	Newborns exposed to vaccine had 10% lower **small for gestational age**, 25% less **preterm birth**, and 33% less **fetal death**
Dodds JOGC	Canada 2006-09 / Retrospect. Cohort	Maternal influenza immunization (1,957)	No maternal influenza immunization (7,824)	Newborns exposed to vaccine had 20% lower **small for gestational age**, 25% less **low birth weight**

Safety of influenza vaccine

Maternal and fetal safety

Maternal safety

World Health Organization

The **excellent and robust safety profile** of multiple inactivated influenza vaccine preparations over many decades, and the potential complications of influenza disease during pregnancy, support that pregnant women should be vaccinated

Vaccine Adverse Event Reporting System (VAERS) database in USA

Only 20 serious adverse events following administration of trivalent influenza vaccine to an estimated 11.8 million pregnant women

http://www.who.int/vaccine_safety/publications/safety_pregnancy_nov2014.pdf ,

Review by Tamma et al

- 10 observational studies and 2 RCTs
- Among 4400 women given inactivated influenza vaccine at all stages of pregnancy, there was no increase in adverse birth outcomes or congenital fetal anomalies over reported background rates

Tamma PD, Ault KA, del RC, Steinhoff MC, Halsey NA, Omer SB. Safety of influenza vaccination during pregnancy. Am J Obstet Gynecol. 2009, 201:547 -5

Maternal Safety of Trivalent Inactivated Influenza Vaccine in Pregnant Women

James D. Nordin, MD, MPH, Elyse Olshen Kharbanda, MD, MPH, Gabriela Vazquez Benitez, PhD, Kristin Nichol, MD, MPH, MBA, Heather Lipkind, MD, MPH, Allison Naleway, PhD, Grace M. Lee, MD, MPH, Simon Hambidge, MD, PhD, Wei Shi, MPH, and Avalow Olsen, BS

- Assessed the safety of TIV at 3 and 42 days after vaccination in 75,906 vaccinated pregnant women with 147,992 unvaccinated counterparts
- Use of TIV even during first trimester, did not increase vaccine related major adverse events particularly neurological disorders such as Guillain-Barre syndrome, optic neuritis, transverse myelitis, or Bell's palsy
- There was no increase in allergic reactions, cellulitis, seizures, no association with thrombocytopenia

Vaccine 32 (2014) 3122–3127

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Safety of influenza vaccination during pregnancy: A review of subsequent maternal obstetric events and findings from two recent cohort studies

Allison L. Naleway[a,*], Stephanie A. Irving[a], Michelle L. Henninger[a], De-Kun Li[b], Pat Shifflett[c], Sarah Ball[c], Jennifer L. Williams[d], Janet Cragan[d], Julianne Gee[d], Mark G. Thompson[d], for the Vaccine Safety Datalink and Pregnancy and Influenza Project

Maternal obstetric events and influenza vaccination coverage, 2010–2011 season, Pregnancy and Influenza Project (n = 1616)

	Number of cases	Vaccinated cases (%)	Number of control	Vaccinated controls (%)	P - value
Gestational hypertension	117	59%	1499	57%	0.68
Preeclampsia/ eclampsia	96	60%	1520	57%	0.51
Gestational diabetes	192	53%	1424	58%	0.17
Chorioamnionitis	121	56%	1495	57%	0.82

No associations between vaccination and gestational diabetes, gestational hypertension, PE/eclampsia, or chorioamnionitis

Vaccine 31 (2013) 5026–5032

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Risks and safety of pandemic h1n1 influenza vaccine in pregnancy: Birth defects, spontaneous abortion, preterm delivery, and small for gestational age infants☆

Christina D. Chambers[a,b,c,d,h,*], Diana Johnson[a,b], Ronghui Xu[c,d,e], Yunjun Luo[a,b], Carol Louik[f,h], Allen A. Mitchell[f,h], Michael Schatz[g,h], Kenneth L. Jones[a,b,h], the OTIS Collaborative Research Group[1]

1032 subjects

841 vaccinated, 191 not vaccinated

- Birth defects: no difference in both arms
- Spontaneous abortion: The risk of abortion was not increased with vaccination
- Preterm delivery: no difference
- SGA: No evidence of risk

Vaccine. 2014;32:3122–3127

Am J Obstet Gynecol. 2011 Nov;205(5):473.e1-9. doi: 10.1016/j.ajog.2011.06.047. Epub 2011 Jun 21.

Adverse events following administration to pregnant women of influenza A (H1N1) 2009 monovalent vaccine reported to the Vaccine Adverse Event Reporting System.

Moro PL[1], Broder K, Zheteyeva Y, Revzina N, Tepper N, Kissin D, Barash F, Arana J, Brantley MD, Ding H, Singleton JA, Walton K, Haber P, Lewis P, Yue X, Destefano F, Vellozzi C.

Influenza vaccination does not affect the risks for preterm delivery, cesarean section, miscarriage or congenital anomaly

No increase in the incidence of preeclampsia or intrauterine growth retardation

Safety in 1st trimester

- Sheffield et al
- Retrospective cohort study
- 5-year study period, 10,225 women received the seasonal influenza vaccine antepartum; 8,690 of these delivered at the trial site, 439 in the first trimester and 8,251 in the second and third trimesters

Obstet Gynecol. 2012 Sep;120(3):532-7. doi: 10.1097/AOG.0b013e318263a278.

Effect of influenza vaccination in the first trimester of pregnancy.

Sheffield JS[1], Greer LG, Rogers VL, Roberts SW, Lytle H, McIntire DD, Wendel GD Jr.

	Still birth	Neonatal death	Premature delivery
Vaccine in 1st trimester	0.3%	0.2%	5%
No vaccine	0.6%	0.4%	6%
P value	0.9	0.01	0.004

Influenza vaccination in the first trimester was not associated with an increase in major malformation rates and was associated with a decrease in the overall stillbirth rate

Fetal safety

- Heinonen et al
- Collaborative perinatal project conducted in 1959 through1965 in which >2000 pregnant women were enrolled
- Of those women, nearly 1/3rd were vaccinated during 1st trimester
- Seven year follow-up of the offspring revealed no increased incidences of stillbirth, congenital anomaly, malignancies, or neurocognitive disorder

Challenges in vaccination

Translating recommendations into reality

Vaccine	During pregnancy
Hepatitis A	Yes, if at risk
Hepatitis B	Yes, if at risk
HPV	No
Influenza TIV	**Yes**
Influenza LAIV	No
MMR	No
Meningococcal	If indicated
Pneumococcal	If indicated
Tetanus/ diphtheria Td	Yes, Tdap preferred if >20 wk gestation
Tdap	Yes, preferred
Varicella	No

ACIP 2012

Vaccine	After pregnancy
Hepatitis A	Yes, if at risk
Hepatitis B	Yes, if at risk
HPV	**Yes**
Influenza TIV	**Yes**
Influenza LAIV	**Yes**
MMR	**Yes, give immediately postpartum if susceptible to rubella**
Meningococcal	If indicated
Pneumococcal	If indicated
Tetanus/ diphtheria Td	Yes, Tdap preferred
Tdap	Yes, preferred
Varicella	**Yes, give immediately postpartum if susceptible**

Co-administration

- ACOG: Co-administration of indicated inactivated vaccines during pregnancy or postpartum (Tdap and influenza) is acceptable, safe, and may optimize immunization efforts

Postpartum vaccination

- Capture patients while still in hospital
- Safe to vaccinate in postpartum period, even while breastfeeding
- Tdap and influenza vaccine should be administered if previously not given
- MMR if not previously given should also be administered
- HPV vaccine can also be given safely during lactation

Barriers to vaccination

- Lack of awareness about seriousness of influenza in pregnancy and complications
- Lack of knowledge about guidelines
- Non –interventionist approach to pregnancy especially in 1st trimester
- Belief that vaccine is harmful
- Fear of litigation
- Belief that this is an industry –driven thrust

Strategies to improve vaccination

- Policy
- Reduction in cost
- Education of medical community and patients

Key messages

- Pregnant women are at high risk for serious complications due to influenza virus infection
- Considerable evidence suggests that influenza vaccination is safe at any stage of pregnancy
- Vaccination improves maternal and fetal outcomes
- Excellent and robust safety profile with no increase in adverse events
- Vaccination does not increase the risk of major maternal or fetal complications in pregnancy

Key messages

- Maternal antibodies following vaccination (placental and breast milk) extend protection to newborn through the first 6 months of life
- Maternal vaccination is a cost-effective and targeted strategy to improve pregnancy outcomes in developed and developing countries
- All international health agencies recommend influenza vaccination during pregnancy

Thank you