

# Is TT Immunization in Pregnancy Enough in Indian settings?

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## Abstract

India has a fairly large share in the maternal mortalities of the world. There are many aspects of a healthy pregnancy and immunization is one of them. Maternal immunization protects not just the mother but also imparts protection to the newborn. India introduced TT immunization for pregnant females in 1983. Due to sustained efforts of healthcare providers, training of nurses and midwives about clean delivery practices, strong campaigning of institutional deliveries, maternal and neonatal focused programs and a good coverage of pregnant women with TT immunization - India was finally declared free of maternal and neonatal tetanus on 15th May, 2015. Pertussis continues to be a serious public health problem in India. Pertussis is more dangerous in infancy and leads to substantial morbidity and mortality. The damage is particularly higher when the infant is only weeks old and still haven't received the primary immunization. Thus there is a need to introduce Tdap vaccine for pregnant women so that pertussis burden in infancy can reduce. An important cause of morbidity and mortality in pregnancy is influenza. Thus, influenza vaccine is the second vaccine that needs to be given to pregnant women.

**Keywords:** Maternal mortality; Tdap; Influenza; Neonatal tetanus; Maternal tetanus

## Pregnancy – Physiological State Surrounded by Pathologies

Pregnancy is a physiological state yet is vulnerable at all stages. Many infections like Hepatitis E and influenza- that are rather mild otherwise cause increased mortality during pregnancy. Viral infections like rubella and chickenpox- that can clearly be given a miss otherwise can create havoc on the development of the fetus leading to major congenital deformities. India has a fairly large share in the maternal mortalities of the world. Though the maternal mortality rate has reduced from 212 deaths per 100,000 live births in 2007 to 178 deaths in 2012, there is still a long way to go [1]. In India, the major causes of maternal mortality are bleeding, sepsis, unsafe abortions, eclampsia, obstructed labor, anemia, malaria and heart disease [2]. There are many aspects of a healthy pregnancy and immunization is one of them. Immunization protects not just the mother but also imparts protection to the newborn. Antibodies are passed to the neonate that fights diseases till the baby is old enough to get the first immunization.

Vaccination is a proven and one of the most cost-effective child survival interventions [3]. All countries in the world have an immunization program to deliver selected vaccines to the targeted beneficiaries, specially focusing on pregnant women, infants and children, who are at a high risk of diseases preventable by vaccines [4]. Pertussis in adolescents and adults is a major problem that goes undetected and is responsible for considerable morbidity in these age groups. Pertussis also serves as a reservoir for disease transmission to unvaccinated/partially vaccinated young infants [5]. Just like pertussis, influenza is another neglected disease in pregnancy, though it has been associated with considerable morbidity and mortality [6].

## Tetanus Story – A Long Battle Well Fought

It was estimated that maternal tetanus accounted for about 5% of maternal mortality in India, or 15,000–30,000 deaths every year [7]. Similarly, neonatal tetanus also accounted for many deaths (200,000 in 1980s). Thus Tetanus toxoid (TT) immunization was introduced for pregnant women in Expanded Program on Immunization (EPI) in 1983 [8]. Due to sustained efforts of healthcare providers, training of nurses and midwives about clean delivery practices, strong campaigning of institutional deliveries, maternal and neonatal focused programs and a good coverage of pregnant women with TT immunization - India was finally declared free of maternal and neonatal tetanus on 15th May, 2015 [9]. Since neonatal tetanus (NT) is linked to the immunization status of mothers, elimination of NT has been adopted as a proxy for the elimination of maternal tetanus [7]. However, the efforts should not stop at eliminating tetanus and emphasis should be laid on other infectious diseases that affect expectant mothers, fetuses and newborns.

## Pertussis – An Unidentified Killer

Pertussis was once a major killer of infants but the global incidence declined with the introduction of whole cell pertussis (wP) vaccine in 1970s. Later it was found that the whole cell component was causing adverse effects following immunization, so in 2009, acellular pertussis (aP) vaccine was introduced to reduce the adverse effects [10]. Since then outbreaks of pertussis have been reported from many industrialized countries, which boast of high immunization coverage with aP vaccine [11-13].

There can be multiple factors playing a role in this- for example improved case reporting, better diagnostic techniques, increased awareness and sub-optimal efficacy of aP vaccine as compared to wP vaccine [14-17]. Currently, pertussis in adolescents and adults is responsible for considerable morbidity in these age groups and also serves as a reservoir for disease transmission to unvaccinated/partially vaccinated young infants [5]. The major reason for the high burden of pertussis in older age groups is that the immunity imparted by pertussis vaccine is not life long and there has been an observation that immunity wanes with both wP and aP vaccines [18]. According to few studies the protection accorded by wP vaccines wanes by 50% over a period of 6-12 years. Whereas little is known about the duration of protection following aP vaccination in developing countries, many studies in industrialized world documented faster waning with aP vaccines and showed that protection waned after 4-12 years [19-25]. This has led to the increase in incidence of pertussis in both infants and adults.

Pertussis continues to be a serious public health problem in India [10]. Pertussis is more dangerous in infancy and leads to substantial morbidity and mortality. The damage is particularly higher when the infant is only weeks old and still haven't received the primary immunization [26]. Indian Academy of Pediatrics (IAP) believes that pertussis is a highly prevalent pediatric illness having significant morbidity and mortality in the country [10]. Though reliable data on exact burden and incidence of pertussis in the country are scarce, and laboratory confirmation is not readily available, pertussis is widespread [10].

Tetanus, diphtheria and acellular pertussis (Tdap) immunization during pregnancy appears to be most effective strategy to have the most impact on infantile pertussis, especially during the first few weeks after birth [27]. Vaccination of pregnant women has a good likelihood of preventing pertussis in very young infants, without the risk of just increasing it at a later age. So, the strategy of vaccinating pregnant women may be effective [10,26]. There is no data on the coverage of Tdap in adolescents and adults in India since it is being used exclusively in private health sector [10]. In 2011, the Advisory Committee on Immunization Practices (ACIP) recommended a dose of Tdap to all pregnant women after 20 weeks gestation to provide protection for both the mother and her newborn during the infant's earliest weeks of life [28]. IAP therefore now suggests immunization of pregnant women with a single dose of Tdap during the third trimester (preferred during 27 through 36 weeks gestation) regardless of number of years from prior Td or Tdap vaccination. Tdap has to be repeated in every pregnancy irrespective of the status of previous immunization (with Tdap). Even if an adolescent girl who had received Tdap one year prior to becoming pregnant will have to take it since there is rapid waning of immunity following pertussis immunization [10]. Though optimal timing for administration is between 27 and 36 weeks of gestation, Tdap may be given at any time during pregnancy [29].

#### **Tdap Vaccination – an Additional Benefit for Adults**

Tdap vaccination will not only impart protection to

neonates against pertussis and diphtheria but will also protect the mothers against these diseases. Adults in India are susceptible to tetanus, diphtheria and pertussis and covering antenatal women will cover a substantial proportion of population and will help in bringing down the cases in the community. Though the exact prevalence is not known but a few studies have been done. A study done on seroprevalence of antibodies against tetanus, diphtheria and pertussis among 62 adults in Pune, India revealed that though majority of participants had protective antibodies against tetanus and diphtheria but only 74% and 9% of them had long-term protection, respectively [30]. For pertussis, more than 50% had no seroprotection. A study in Delhi among a random sample of healthy adults reported that 53% of adults were unprotected; 22% were seen to have only a basic protection against diphtheria; 25% were protected against both diseases; 47% were susceptible to tetanus [31]. A large prospective study done between 2017-2010 in various European countries showed the incidence of recent pertussis infection among adults to be 3% [32]. However, it has also stated that pertussis infection in adults is majorly under reported and under diagnosed. Thus the Indian adults are susceptible to these diseases and booster doses of vaccination in adulthood are necessary.

In India, One dose of TT is routinely given at age 10 And 16 years of age. However, people who do not get Tdap at that age should get it as soon as possible. Tdap is especially important for health care professionals and anyone having close contact with a baby younger than 12 months.

#### **Influenza in Pregnancy- Neglected but Important**

Another neglected disease in pregnancy is Influenza, though it has been associated with considerable morbidity and mortality [6]. Historically in the 1918 pandemic, it was seen that the overall mortality among pregnant females who developed influenza-associated pneumonia was 27% and it exceeded 50% in the third trimester of pregnancy [33]. In the 2009 pandemic, pregnant women accounted for 6% of influenza related hospitalizations, ICU admissions, and deaths [34,35]. In the age group of 18-29 years, pregnancy accounted for up to 29% of influenza-associated hospitalizations and 16% of deaths [36-38]. In a systematic review of 100 studies (1961- 2015), it has been reported that pregnant women are more often admitted to intensive care unit due to influenza virus infection [39]. It has also been reported that pregnant women are 7.2 times more likely to be hospitalized and 4.3 times more likely to be admitted to an ICU than other women [40]. Influenza has also been associated with 5-fold increase in perinatal mortality causing miscarriages, stillbirths, and early neonatal diseases and deaths [41,42]. A 3-fold increased risk of premature and complicated birth was observed in pregnant women hospitalized with A/H1N1pdm09 [43].

There are limited data describing the burden of influenza in pregnancy in India [6]. However, few sporadic studies can be found. A study done in north India in 2015 on 266 pregnant females was done to assess the contribution of influenza to acute respiratory illness (ARI) in pregnancy [6]. Two Twin

nasopharyngeal/oropharyngeal swabs were obtained and tested for influenza viruses by RT-PCR technology. It was seen that 50 (18.8%) patients tested positive for influenza. Influenza positive patients were suffering more from rigors and headache. Though Oseltamivir and supportive therapy were administered to all confirmed cases, 9 influenza positive cases needed hospitalization for their respiratory illness, and 5 developed respiratory failure. Of these, 4 (3 in third trimester) succumbed to their illness. Thus it was observed that influenza viruses are a cause of significant morbidity and mortality among pregnant females with ARI in north India. In spite of high rate of morbidity and mortality, uptake of influenza vaccination in pregnant females is very low [5].

Since 2004, the ACIP and the American College of Obstetricians and Gynecologists (ACOG) have recommended influenza vaccination for all women of Americas who are or will be pregnant regardless of trimester of pregnancy [44,45]. In India, Federation of Obstetric and Gynaecological Societies of India (FOGSI) have recommended Influenza vaccination for mothers from 26 weeks onwards [46]. Influenza vaccine can help in improving the maternal mortality statistics. However, India is still a long way from introducing influenza vaccine in the National Immunization Schedule as it is still grappling with the low immunization coverage of children. Also, appropriate preventive strategies of influenza vaccination and early initiation of antiviral therapy during illness should be stressed upon [6]. The various hurdles in introducing additional vaccines for expectant mothers are shortage of funds, lack of awareness about adult immunization, paucity of studies supporting such immunization in the Indian subcontinent and sole focus of government on childhood vaccination. However, apart from the additional costs of vaccines and awareness generation, there is no need to expand manpower or infrastructure as the same is already in place for pregnant females and they are being routinely immunized.

### Way forward

Women do not fully avail the health services that are meant for them. They are often busy in household chores and they neglect their own health. A study done in Delhi on 358 pregnant women revealed that though 80% women suffered from some morbidity but overall care sought during pregnancy was poor [47]. The recommended 3 antenatal visits were also not made by many women. Thus to reduce morbidity and mortality it is important that women are mobilized to utilize health services. Schemes like Janani Suraksha Yojna and Janani Shishu Suraksha Karyakram are welcome ways to bring focus on reducing out of pocket expenditures during and after delivery. Grass root level workers should encourage more and more pregnant women to avail health services. Important modes of imparting health education like television and radio should target this group and spread awareness regarding illnesses that have adverse effects in pregnancy. Much needed vaccines like Tdap and Influenza should be added in national immunization schedule and women should be immunized at the first point of contact like sub center, primary health center or maternal and child health center.

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