GLOBAL JOURNAL OF MEDICINE AND PUBLIC HEALTH

Assessment of burden of seasonal influenza in India and consideration of vaccination policy

Mahima Venkatesh[*1], *Charles R Doarn* [2], *Mark Steinhoff* [3], *Jun Ying* [4]

ABSTRACT

This study summarizes the burden of seasonal influenza and the surveillance of the disease in published literature in India. This will determine the need for vaccination policy changes, especially in regards to pregnant women. A systematic literature review was conducted in PubMed, SCOPUS, and EMBASE to identify studies in India that were published until February 28, 2015 and described the burden of seasonal influenza. The search terms used included "influenza", "seasonal", and "India". Peak influenza activity was observed from June to August in Northern India and October to December in Southern India. Studies showed the importance of multi-site investigations due to differences in incidence and patient characteristics. During the peak rainy season, influenza accounted for 20-42% of monthly acute medical illness hospitalizations. Genetic drifts and varying seasonality in different parts of the country are challenges that are faced when attempting to control influenza. While many obstetricians believed that influenza could have severe consequences for themselves and their patients, most did not get vaccinated. Reasons for not getting influenza vaccine included ignorance about availability, skepticism about efficacy, busy schedule, fear of side effects, perception of not being at risk, and the belief that vaccine programs are motivated by profit. The data suggest that influenza is a substantial contributor to severe respiratory illness. There is a need for more large-scale studies over a broader geographical range in India. In order to improve vaccination rates, there must be a national vaccination policy as suggested by the literature, especially for high-risk groups such as medical practitioners and pregnant women. Also, the antigenic drifts of circulating influenza viruses in India combined with the temporal peak in seasonality in various parts of the country demonstrate a need for regional vaccination policy.

GJMEDPH 2016; Vol. 5, issue 5

[1]College of Medicine, University of Cincinnati

[2]Department of Family and Community Medicine, University of Cincinnati

[3]Cincinnati Children's Hospital Medical Center

[4]Department of Environmental Health, University of Cincinnati

***Corresponding Author:**
Mahima Venkatesh
College of Medicine, University of Cincinnati, Ohio
venkatmb@mail.uc.edu

Conflict of Interest—none

Funding—none

INTRODUCTION

The global annual attack rate of influenza is estimated at 5%–10% in adults and 20%–30% in children.[1] Worldwide, these annual epidemics are estimated to result in about 3 to 5 million cases of severe illness and about 250,000 to 500,000 deaths.[1] Influenza epidemics also take an economic toll by lowering productivity of the workforce and taxing limited health services.

Influenza is a viral infection, affecting mainly the nose, throat, and bronchi. Most infected individuals do not require medical treatment and recover within one to two weeks. However, infection can lead to severe complications of underlying conditions, including pneumonia and death, especially in children, the elderly, pregnant women and those with other serious medical conditions.[1] More than 90% of influenza-related deaths occur in patients in the older age group. Underlying medical conditions that

increase the risk of hospitalization include diabetes and cardiovascular, neurological and chronic respiratory diseases, such as asthma.[2]

The most effective method of preventing influenza infection is through vaccination. Safe and effective influenza vaccines are available and have been used worldwide for more than 60 years. Among healthy adults, influenza vaccine provides adequate protection. Among the elderly, the vaccine tends to be less effective in preventing illness. However, it may reduce severity of disease and incidence of complications and deaths.[2]

Vaccination is especially important for people at higher risk of serious influenza complications, and for people who live with or care for high-risk individuals. The World Health Organization (WHO) recommends annual vaccination for pregnant women at any stage of pregnancy, children aged six months to five years of age, elderly individuals (≥65 years of age), individuals with chronic medical conditions, and healthcare workers.[1] Pregnant women are at risk for severe complications or death from influenza. Studies around the world have shown that vaccination protects the mother and the child. It protects fetal development from negative effects of influenza infection and provides protection in infants for the first six months after birth.[3] Several studies have shown that the inactivated vaccines have been shown to be safe and effective in pregnant women and their offspring when given at any trimester.[3]

Of all of the infectious diseases, influenza needs specific strategy due to its high rate of antigenic change. The vaccine changes every year because the vaccine antigens are modified to match with new circulating viruses.[1] The seasonality of influenza in the tropics also complicates vaccination timing. In temperate regions, infection rates peak during the winter months. However, in tropical and subtropical areas, some areas have year-round circulation while others have biannual peaks.[4] One study of tropical and subtropical countries of southern and south-eastern Asia that lie north of the equator showed that tropical and subtropical countries exhibited influenza activity peaks that were earlier than temperate climate countries north and south of the equator.[5]

Fig 1 Map of India with States Delineated

India, the world's second-most populous country, accounts for 20% of global childhood deaths from respiratory infections.[6] Research on the seasonality within India has been influential to determine the peak season and proper timing of the influenza vaccination. There are discrete seasons that vary greatly from northern to southern. For example, Jammu and Kashmir, the northernmost states of India, have severe winters from December to March, whereas Delhi, the capital region, has milder winters.[7] The Indian Academy of Pediatrics (IAP) notes that there is usually limited influenza activity seen throughout the year in India with a clear peaking during the local rainy season.[8] The rainy season in the country lasts from June to August in all the regions except Tamil Nadu where it occurs from October to December. IAP recommends that the ideal time for vaccination should be before the onset of the rainy season.[1] Recent research shows that India has distinct seasonality different from other northern hemisphere countries that might be related to latitude and environmental factors. Recent research shows that India has distinct seasonality different from other northern hemisphere countries that might be related to latitude and environmental factors. Studies by Chadha et al in 2015, showed that there are three major patterns of influenza circulation in India. In Srinagar, the peak influenza is during the winter (January-April). The peak influenza activity is from June-October in Delhi, Dibrugarh, Lucknow, Kolkata, Nagpur, Pune, and Alappuzha, with minor peaks during winter time and a late monsoon related peaks in Chennai and Vellore from September to December.[9]

The IAP's most recent recommendations for the influenza vaccine, focuses only on the category of "high-risk children." [8] Unlike the United States (U.S.) and WHO, the IAP states several reasons why it has not offered universal recommendations for the vaccine.[8] They believe that the burden is not well defined and there is insufficient data to estimate precisely the contribution of influenza to childhood hospitalization and mortality. In their opinion, there is no justification to prioritize strategies for influenza prevention and control.[8] They say that the burden of H1N1 is "so small" when compared with diseases such as tuberculosis, which affected 2.1 million people in 2013.[10]

The WHO National Influenza Centres in India also report that despite 50 years of global influenza pandemic and epidemic investigations, there is a need to expand influenza surveillance within India. Currently, there are only a few centers researching these types of studies within India.[11] Systematic laboratory-based surveillance of influenza viruses has been carried out in limited sites in varied regions in India. There is also the India Influenza Network, comprised of 10 sites located in major areas of India.[12]

There is still very limited data available about the annual cases and deaths due to influenza in India. Moreover, while the influenza vaccine has been in the Indian market since 2004, there is no published data on safety, tolerability, and effectiveness of the vaccine for Indian children.[10] There is a need to clearly assess the burden of influenza in India and consider changes to current Indian government policies regarding influenza vaccination. This paper provides background information on the burden of influenza, especially related to maternal health. Also, it will investigate the current IAP and Indian government policies on influenza vaccination and determine if there is a need to change the policies and recommendations.

METHODS

A systematic literature review was conducted using PubMed, SCOPUS, and EMBASE to identify studies in India that were published up to February 28, 2015 and described the burden of seasonal influenza. The search terms used included "influenza", "seasonal", "pregnancy", and "India". Duplicates were eliminated from the list of journal articles. Once the articles were identified, titles and abstracts were screened for relevance. Any articles that did not focus on seasonal influenza in India or mainly focused on pandemic influenza were excluded. Review articles, case reports, and editorial articles were also excluded. Finally, the references section of all selected articles was examined to identify additional articles.

The PubMed search resulted in 75 results. The SCOPUS search resulted in 135 paper publications. The EMBASE search resulted in 163 results. After reviewing the articles, 19 papers were selected and split into categories of: Burden of Disease, Surveillance, and Vaccines. One review article on influenza and pregnancy was kept and discussed in the Pregnancy section. All inclusion and exclusion criteria as well as the categorical method were predetermined after discussion and consensus among coauthors. The search was conducted by the lead author of this study."

RESULTS

Burden of Disease

The burden of respiratory virus-associated illness in India is largely unknown, especially in children. In a 2013 study, Broor et al. estimated the incidence of respiratory virus associated hospitalizations among children aged less than five years.[14] This was based on a population-based surveillance of 9,500 children for hospitalizations for acute medical illness in rural northern India and testing for respiratory viruses by real-time reverse transcription polymerase chain reaction (rRT-PCR). Influenza accounted for 7% of all hospitalizations in 2007 in Delhi. Influenza virus detection peaked in this region during the rainy season in June-July when influenza accounted for 20-42% of monthly acute medical illness hospitalizations.

One study, conducted by Chadha et al., documented active surveillance for hospitalized patients with acute medical illnesses or acute chronic disease exacerbations in Pune during pandemic and post pandemic periods (May 2009–April 2011).[15] Chadha et al. found that the average annualized incidence of influenza-associated hospitalizations in a current study was 44.1 per 10,000 persons, which is substantially higher than 3.6–11.5/10,000 persons reported in the U.S.[15] Among 9,426 hospitalizations, 3,391 (36%) patients were enrolled; 665 of 3,179 (20.9%) tested positive for influenza. Of 665 influenza positives, 340 (51%) were pandemic A (H1N1) pdm09 and 327 (49%) were seasonal. The proportion of patients with influenza peaked during August 2009 (39%) and 2010 (42%). The seasonal hospitalized influenza disease was highest in the 5–29 year olds.

Another study by Koul et al. from 2011, looked at the prevalence and clinical presentations of seasonal and pandemic influenza viruses among acute respiratory illness (ARI) patients from Srinagar, a temperate climate area in northern India, during the peak winter season.[16] Based on 194 individuals presenting with ARI, twenty-one (10.8%, age 15–80 years, median age 40 years) patients tested positive for influenza viruses: 13 (62%) for 2009 A (H1N1) virus, 6 (28.5%) for seasonal influenza A(H3N2), and 2 (9.5%) for influenza B.

Koul et al. from 2015, collected data from prospective surveillance for influenza among patients hospitalized with acute exacerbations of chronic obstructive pulmonary disease (COPD) (AECOPD) to estimate the contribution of influenza to the overall burden of AECOPD at a tertiary care hospital in Kashmir, India.[17] During a 2-year period, influenza was associated with 8% of all hospitalizations for AECOPD at the main tertiary care hospital in Kashmir, India. Patients with influenza were more likely to die during hospitalization (adjusted OR 3.4, CI 1.0–11.4) than those without. In addition, only about 8% of patients in the study reported receiving influenza vaccine. According to the study, this is consistent with limited data on uptake in other high-risk groups in India.

Chaudasama et al., published in 2013, considered 1,726 patients suffering from A (H1N1) influenza and seasonal influenza that were admitted in the different hospitals of Rajkot city of Saurashtra region between September 2009 and February 2011.[18] Among the patients hospitalized due to influenza, 29.6% (511/1,726) were laboratory confirmed cases of A (H1N1) influenza while the rest 70.4% (1,215/1,726) were cases of seasonal influenza. 24.9% (127/511) of those admitted for A (H1N1) influenza died as compared to 5.3% (65/1,215) of those suffering from seasonal influenza.

A 2010 article by Chudasama et al., investigated patients who were hospitalized with 2009 pandemic H1N1 influenza and seasonal influenza in the

Saurashtra region of India.[19] From September 2009 to February 2010, a total of 773 patients with influenza virus attending different hospitals in Rajkot city were studied. Of the 733 patients, 35.4% (274/773) were cases of 2009 pandemic H1N1 influenza and 64.6% (499/773) were cases of seasonal influenza. Of the 274 patients with 2009 pandemic H1N1 influenza, the median age was 29.5 years, and 51.5% were males. The 5.5% prevalence of pregnancy ($p = 0.001$) in this study was higher than the expected prevalence in the general population (1%). This study represents one of the largest investigations involving a series of patients with severe 2009 influenza A (H1N1) infection and seasonal influenza covering two seasons of monsoon and winter. Diabetes mellitus (9.9%) and hypertension (8.8%) were the most common underlying conditions present in the hospitalized patients, in contrast to patients with seasonal influenza and influenza A (H1N1) in the U.S., where asthma and COPD were the most common underlying conditions.

Finally, the last study by Hirve et al., published in 2014, was a prospective facility-based surveillance for all hospitalizations at 72 health facilities.[20] Health utilization surveys were conducted in two rural Indian health and demographic surveillance system sites at Ballabgarh and Vadu, in the Maharashtra state, from 2010-2012. During 2010-2012, 6,004 patients hospitalized with acute medical illness were enrolled at study facilities, including 1,717 (29%) patients in Ballabgarh and 4,287 (71%) in Vadu. Compared to Ballabgarh, a higher proportion of patients at Vadu had respiratory specimens positive for influenza viruses (5%, 85/1,717 vs. 21%, 892/4,287, $p < 0.01$). The researchers found differences in both incidence and patient characteristics between communities highlighting the importance of a multi-site approach to estimating national influenza disease burden.

Surveillance

One of the first surveillance studies was published in 1993 based on continuous surveillance of influenza in Pune, India from 1978 and 1990.[21] There were 16 outbreaks during this time and 10 of them were during the rainy season. Two hundred and ninety isolates consisting of several antigenic variants of influenza type A (H_3N_2), type A (H1N1) and type B viruses were identified. Seasonal analysis indicated that the highest number of isolates was collected during the rainy months of July, August, and September. The study also demonstrated that rainfall, relative humidity, and small differences between minimum and maximum temperatures influenced the occurrence of influenza outbreaks in the rainy season but that other unidentified factors may also be involved.

Agrawal et al. in 2010, implemented influenza surveillance in eastern India in 2005 to identify circulating subtypes and characterize their generic diversity.[22] During the study period, there was a persistence of H_3N_2, with an emergence of H1N1 in late 2006. It began to disappear in late 2007 and no A/H1N1 was detected in 2008. It re-emerged and co-circulated with both H_3B_2 during 2009.

Roy et al. in 2011, characterized the genetic diversity of circulating influenza B viruses in Kolkata, India.[20] Unlike Influenza A, Influenza B viruses evolve at a slower rate and do not have multiple HA and NA subtypes. One mechanism of generating genetic diversity is by amino acid substitution and re-assortment.

Agrawal et al., published in 2009, was one of the first reports of a systemic surveillance of respiratory viruses with seasonal correlation and prevalence rates from eastern India.[24] It is also believed to be the first report providing seasonal correlation and a prevalence rate for respiratory viruses in children from eastern India. A total of 1,091 respiratory samples were examined from children with suspected acute respiratory tract infections between January 2007 and December 2008. Overall, Influenza A (IAV), Influenza B (IBV) and respiratory syncytial virus (RSV) were detected in 121 (11.09 %), 59 (5.41 %) and 95 (8.71 %) samples, respectively. IAV correlated positively and RSV negatively with rainfall and temperature. This 2-year comparative analysis also confirmed the feasibility of using qPCR in developing countries, which will not only improve the scope for prevention of epidemics, but will also provide crucial epidemiological data from tropical regions.

Another study by Broor et al. published in 2012,

conducted influenza surveillance of patients with influenza-like illness at an Employee Health Clinic (EHS) at All India Institute of Medical Sciences (AIIMS), New Delhi and pediatric out-patient department of civil hospital at Ballabhgarh, under the Comprehensive Rural Health Services Project (CRHSP) of AIIMS, in Delhi region from January 2007 to December 2010.[22] Of the 3,264 samples tested, 541 (17%) were positive for influenza viruses, of which 221 (41%) were pandemic Influenza A (H1N1) pdm09, 168 (31%) were seasonal influenza A, and 152 (28%) were influenza B. Influenza viruses were detected year-round and the types drastically varied. In 2007, there was an equal distribution of seasonal A (H1N1) and influenza B. In 2008, influenza B was dominant. At the beginning of 2009, a circulation of influenza A (H3N2) viruses was observed, which was followed by an emergence of Influenza A (H1N1) with co-circulation of influenza B viruses. In early 2010, influenza B was a dominant subtype with second wave of H1N1 in August- September 2010. The peaks of influenza coincided with the local monsoon months, followed by minor peaks in winter at both urban and rural sites.

A study published in 2011 by Chadha et al., initiated a multisite human influenza surveillance network in 2004.[26] From September 2004 to December 2008, 617 (4.43%) of 13,928 cases yielded isolates: 27.8% were influenza A (H1N1), 29.8% were type A (H3N2), and 42.3% were type B. The yearly type and subtype distribution varied significantly from site to site. Peak influenza activity was observed during local monsoons from June to August in Delhi, Pune, and Kolkata and October to December in Chennai.

A study published in 2012 by Hirve et al., assessed case definitions for influenza in Vadu, Maharashtra State, India.[27] Of the 2,179 patients included in the final analysis, 21% were PCR-positive for influenza virus, 96% reported fever and 4% reported shortness of breath. The WHO case definition for sever acute respiratory illness had a sensitivity of 11% among patients aged less than 5 years and 3% among older patients. When shortness of breath was excluded from the definition, the sensitivities increased to 69 and 70% respectively. The inclusion of shortness of breath may grossly underestimate the burden posed by influenza in hospitals. The exclusion of this from the definition and the inclusion of "cough and measured or reported fever" may improve estimates of the burden.

Another study on the case definitions for influenza was conducted by Gupta et al. and published in 2012.[13] During the period July 2009–August 2011, a research team collected clinical data and specimens from rural patients hospitalized for acute medical illnesses in Ballabgarh, India. Case definitions including only measured fever had lower sensitivity. Measured fever plus cough or sore throat and fever plus either cough, sore throat, runny nose, difficulty breathing, or earache with measured reported fever provided good balance between sensitivity and specificity among hospitalized patients. The simpler case definition of measured reported fever plus cough is suited for field surveillance.

A study published in 2013 by Mukherjee et al., looked at 2,737 patients with acute respiratory infection from the outpatient departments as well as admitted patients in Kolkata, India.[28] The majority of the patients were under five years of age. Out of 2,737 patients enrolled in this study, 59% were found positive for one or more respiratory viruses. Influenza B infection was detected in 12% of patients followed by influenza A (11.7%), respiratory syncytial virus (7.1%), parainfluenza virus-2 (6%), metapneumovirus (3%), parainfluenza virus-3 (1%), parainfluenza virus-4 (0.6%), parainfluenza virus-1 (0.3%), influenza C (0.2%) and human rhinovirus (0.2%). There was a distinct seasonal infection related to monsoon only for influenza A and influenza B viruses.

A study published in 2014 by Dangi et al., planned to determine the pattern of influenza virus activity in Lucknow, India between August 2010 and September 2012.[29] Influenza positivity was 15.8% (423/2,669) in symptomatic patients. Of the 423 total positives, 192 (7.2%) were influenza A and 231 (8.7%) were influenza B. Positivity for influenza virus was significantly (P=0.001, OR=2.9, CI=1.94.3) higher in patients with Influenza like illness (ILI) (17.4%, 396/2,271) than those with severe acute respiratory illness (SARI) (6.8%, 27/398). Influenza A positive samples were subtyped as; pdmH1N1 (67.2%,

129/192) and seasonal H3N2 (32.8%, 63/192). It significantly correlated with monsoon monthly mean rainfall, humidity and dew point while atmospheric pressure was inversely related.

Surveillance

One study by Bali et al., published in 2012, explored the knowledge, attitudes and practices associated with influenza vaccination in healthcare workers in northern India.[30] Only 62 (4.4%) of the healthcare workers had ever received influenza vaccination even as 1,348 (95%) believed that influenza poses adverse potential consequences for themselves or their contacts. About 1,144 (81%) were aware of a vaccine against influenza and 830 (58%) of its local availability. Reasons cited by 1,359 participants for not being vaccinated included ignorance about vaccine availability (435; 32%), skepticism about efficacy (248; 18%), busy schedule (166; 12%), fear of side effects (70; 4%), and a perception of not being-at-risk (82; 6%). Sixty-one percent (865) believed that vaccine programs are motivated by profit.

Another study published in 2014 by Koul et al., studied the uptake of influenza vaccination among pregnant women in northern India and physicians' beliefs and practices regarding vaccination.[4] Among 1,000 women aged 18–41 years (13.6% first trimester, 26.8% second trimester), none had been offered or received influenza vaccination. Only nine (10.0%) of 90 obstetricians surveyed had been vaccinated for influenza in the past five years, although 81 (90.0%) believed that influenza could have severe consequences for themselves and their patients. The reasons cited for non-vaccination included poor knowledge about availability of vaccine and concerns about its efficacy. A majority (79 or 87.8%) believed that vaccination programs are motivated by profit.

A third study, published in 2012 by Bhaskar et al., observed the vaccination rates among pregnant women in Chennai during two months following the availability of influenza vaccine in the region.[31] 140 pregnant women were interviewed during the study period. The mean age of study participants was 25 years (range 21-35 years). Thirty-two (22.8%) were given advice to get vaccinated for pandemic influenza of which 18 (12.8%) received the vaccine. None of them reported to have asked their healthcare provider about the need for influenza vaccination in pregnancy. None of them reported to have received an advisory from the communication media (newspaper, radio or television). Reason for noncompliance among 14 unvaccinated women who were advised to receive the vaccine were (1) fear of complications due to the vaccine (n=4); (2) unawareness of the location of vaccine availability (n=4); and (3) unawareness of the benefit of vaccine (n=4).

Pregnancy

Bhalerao-Gandhi et al. (2015) identified eight Indian studies describing influenza burden and/or outcomes among pregnant women with influenza.[32] In most studies, influenza A (pH1N1) was associated with increased maternal mortality (25–75%), greater disease severity, and adverse fetal outcomes as compared to non-pregnant women. Three of 8 studies reported the effect of maternal influenza infection on fetal and perinatal outcomes. These studies reported fetal mortality ranging from 5.5% to 33% and prematurity rates were from 20% to 33%. Influenza-related maternal mortality ranged from 25% to 70% among pregnant women.

DISCUSSION

Based on the literature review there are several major points that can be drawn from the data. The findings from the studies also show that influenza circulation and influenza association hospitalization should be a major public health concern in India. The data suggest that influenza is a substantial contributor to severe respiratory illness and hospitalization.

Another main point is that there is a need for more large-scale studies over a broader geographical range in India. The studies also should be over a longer period of time to understand the seasonal infection pattern more clearly. Multi-site studies also help to account for variability between locations. Surveillance for seasonal influenza infections along with higher quality prospective studies in pregnant women is needed. Because only few cultures of flu are done, especially in children, there is very little data on the true incidence and impact of influenza infections.

The IAP also says that the target groups for vaccination are not well defined.[8] There are also issues related to vaccine availability, timing, suitability, and effectiveness. Also, there is a need for a more extensive, region-specific surveillance.[1] There is limited data from India on the mutations and virus subtypes in different regions of the country. This could cause vaccines to be ineffective and could result in future outbreaks.[10] Global formulation of the influenza vaccines may not be useful for India. There is limited data in India and there is a need for more research This will improve the efficacy of the vaccine for the Indian subcontinent population.

There is poor uptake of the influenza vaccine in India. This is detrimental to the high-risk groups, especially pregnant women. Influenza in pregnancy can have substantial effects in both the mother and the fetus, including higher rates of hospitalization. However, influenza has also been associated with adverse fetal outcomes including a higher risk of perinatal death, intrauterine growth restriction, and preterm birth. Evidence also shows that pregnant women have increased susceptibility to complications of influenza, due to various physiologic and immunologic changes associated with the state of pregnancy. Studies have shown that maternal influenza vaccination and naturally occurring maternal antibodies against influenza have been reported to protect newborns during the first few months of life. This protective effect has also been shown with breastfeeding. While many argue that the number of pregnant women who are hospitalized due to influenza is small and mass vaccination is not necessary, high mortality rates have been shown especially during pandemics. While physicians believe that influenza is an infection with potentially serious consequences, many do not recommend or offer it to their patients, especially pregnant women. This is due to misconceptions about the vaccine efficacy, safety and necessity. Many patients also do not have adequate knowledge about influenza.

The WHO recommends that pregnant women should have the highest priority for influenza vaccination when countries consider the initiation or expansion of vaccination programs.[32] Effective communication strategies and educational programs will be necessary to introduce the vaccine to healthy younger populations, including pregnant women and young children. Year-round availability of the vaccine, especially for pregnant women is crucial. This must be combined with influenza surveillance and pandemic preparedness strategies. The WHO also recommends modeling of the economic consequences of vaccination in the risk groups, particularly in low- and middle-income countries.[33]

Especially in countries with limited resources such as India, reduction of preterm birth through influenza vaccination interventions can reduce the overall infant mortality rate at the population level. Influenza during pregnancy has negative effects in the mother, fetus and infant, with possible consequences into adulthood of the child.[33]

In order to improve vaccination rates, there must be a national vaccination policy as suggested by the literature. While it may not be practical to recommend routine influenza vaccination in the general population of 1.2 billion in India, the literature suggests vaccinations especially high-risk groups such as the elderly, children, medical practitioners and pregnant women. This will require education and improving awareness among antenatal care providers and primary care physicians to encourage vaccination. Since India already manufactures influenza vaccine, there should be more push to administer the vaccine in the high-risk groups. Also, the antigenic drifts of circulating influenza viruses in India combined with the temporal peak in seasonality in various parts of the country demonstrate a need for regional vaccination.

REFERENCES

1. "Influenza (Seasonal)." WHO. N.p., Mar. 2014. Web. http://www.who.int/mediacentre/factsheets/fs211/en/ (Last Accessed: January 5, 2015)
2. "Acute Lower Respiratory Infections." European Lung White Book. European Respiratory Society, 2015. Web. http://www.erswhitebook.org/chapters/acute-lower-respiratory-infections/ (Last Accessed: January 5, 2015)
3. "Burden of Influenza." Influenza Foundation of India. N.p., 2015. Web.

http://www.apaci.asia/influenza/burden-of-influenza-a-benefit-of-vaccination (Last Accessed: January 5, 2015)
4. Koul, P. A., Bali, N. K., Ali, S., Ahmad, S. J., Bhat, M. A., Mir, H., & Khan, U. H. (2014). Poor uptake of influenza vaccination in pregnancy in northern India. International Journal of Gynecology & Obstetrics, 127(3), 234-237.
5. Saha, Siddhartha et al. "Influenza Seasonality and Vaccination Timing in Tropical and Subtropical Areas of Southern and South-Eastern Asia." Bulletin of the World Health Organization 92.5 (2014): 318–330. PMC. Web. 10 Feb. 2016.
6. "Visits Highlight the Importance of CDC's Influenza Activities in India." Centers for Disease Control and Prevention. Centers for Disease Control and Prevention, 08 Feb. 2012. Web.
7. Koul, P. A., Broor, S., Saha, S., Barnes, J., Smith, C., Shaw, M., Chadha, M., Lal, R. B. (2014) Differences in Influenza Seasonality by Latitude, Northern India. Emerging Infectious Diseases 20(10):1723-6.
8. Vashishtha,V. M., Kalra, A., Choudhury, P.. (2013) Influenza Vaccination in India: Position Paper of Indian Academy of Pediatrics, 2013. Indian pediatrics 50(9): 867-74.
9. Chadha, Mandeep S. et al. "Dynamics of Influenza Seasonality at Sub-Regional Levels in India and Implications for Vaccination Timing." PLoS ONE10.5 (2015): e0124122. PMC. Web. 10 Feb. 2016.
10. Pulla, P. (2015) Outbreak of Swine Flu in India Is No Worse than Seasonal Flu, Say Specialists. BMJ h1097
11. Rao, B.L. (2002) Epidemiology and control of influenza. The National medical journal of India. 16(3) 143-149.
12. Chadha, Mandeep S. et al. "Dynamics of Influenza Seasonality at Sub-Regional Levels in India and Implications for Vaccination Timing." PLoS ONE10.5 (2015): e0124122. PMC. Web. 10 Feb. 2016.
13. Gupta, V., Dawood, F. S., Rai S. K., Broor, S., Wigh, R,, Mishra, A.C., Lafond, K., Mott, J.A., Widdowson, M-A., Lal, R. B. & Krishnan, A. (2013) Validity of Clinical Case Definitions for Influenza Surveillance among Hospitalized Patients: Results from a Rural Community in North India. Influenza and other respiratory viruses 7(3): 321-29.
14. Broor, S, Krishnan, A., Roy, D.S., Dhakad, S., Kaushik, S., Mir, M. A., Singh, Y., Moen, A., Chadha, M., Mishra, A.C., & Lal R. B. (2012) Dynamic Patterns of Circulating Seasonal and Pandemic A(H1N1) pdm09 Influenza Viruses From 2007–2010 in and around Delhi, India. PLoS one 7(1), e29129.
15. Chadha, M. S., Hirve, S., Dawood F. S., Lele, P., Deoshatwar, A., Sambhudas S., Juvekar, S., Lafond K. E., Mott, J.A., Lal R. B., Mishra A. C., & Cowling, B. J. (2013) Burden of Seasonal and Pandemic Influenza-Associated Hospitalization during and after 2009 A(H1N1) pdm09 Pandemic in a Rural Community in India. PLoS one: e55918.
16. Koul, P.A., Mir, M. A., Bali, N. K., Chawla-Sarkar, M., Sarkar, M., Kaushik, S., Khan, U. H., Ahmad, F., Garten, R., Lal R. B., & Broor S. (2011) Pandemic and Seasonal Influenza Viruses among Patients with Acute Respiratory Illness in Kashmir (India). Influenza and Other Respiratory Viruses 5(6):E521-527.
17. Koul, P. A. et al. (2015) Contribution of Influenza to Acute Exacerbations of Chronic Obstructive Pulmonary Disease in Kashmir, India, 2010–2012. Influenza and Other Respiratory Viruses 9(1): 40–42.
18. Chudasama, R. K., Patel, U. V.,Verma, P.B., Banerjee, A., Buch, P., & Patel, P. (2013) A Two Wave Analysis of Hospitalizations and Mortality from Seasonal and Pandemic 2009 A (H1N1) Influenza in Saurashtra, India: 2009-2011. Annals of Medical and Health Sciences Research 3(3):334-40.
19. Chudasama, R., Patel, U., & Verma, P. B. (2010) Hospitalizations associated with 2009 influenza A (H1N1) and seasonal influenza in Saurashtra region, India. The Journal of Infection in Developing Countries 4(12):834-841.
20. Hirve, S., Krishnan, A., Dawood, F. S., Lele, P., Saha, S., Rai, S., Gupta, V., Lafond, K. E., Juvekar, S., Potdar, V., Broor, S., Lal, R. B., & Chadha, M. (2014) Incidence of Influenza-associated Hospitalization in Rural Communities in Western and Northern India, 2010–2012: A Multi-site Population-based Study. Journal of Infection 70(2):160-70.
21. Rao, B. L., and K. Banerjee. (1993) Influenza Surveillance in Pune, India, 1978-90." Bulletin of the World Health Organization 71(2): 177–81.
22. Agrawal, A. S, Sarkar, M., Ghosh, S., Roy, T., Chakrabarti, S., Lal R., Mishra, A. C., Chadha, M. S., & Chawla-Sarkar, M. (2010) Genetic Characterization of Circulating Seasonal Influenza A Viruses (2005–2009) Revealed Introduction of Oseltamivir Resistant H1N1 Strains during 2009 in Eastern India. Infection, Genetics and Evolution 10(8):1188-198.

23. Roy, T., et al. (2011) Surveillance and molecular characterization of human influenza B viruses during 2006–2010 revealed co-circulation of Yamagata-like and Victoria-like strains in eastern India" Infection, Genetics, and Evolution 11(7):1595-1601.
24. Agrawal, A. S., M. Sarkar, S. Chakrabarti, K. Rajendran, H. Kaur, A. C. Mishra, M. K. Chatterjee, T. N. Naik, M. S. Chadha, and M. Chawla-Sarkar. (2009) Comparative Evaluation of Real-time PCR and Conventional RT-PCR during a 2 Year Surveillance for Influenza and Respiratory Syncytial Virus among Children with Acute Respiratory Infections in Kolkata, India, Reveals a Distinct Seasonality of Infection. Journal of Medical Microbiology 58(12): 1616-622.
25. Broor, S., Dawood, F.S., Pandey, B. G., Saha, S., Gupta, V., Krishnan, A., Rai, S., Singh, P., Erdman, D., & Lal, R. B. (2013) Rates of Respiratory Virus-associated Hospitalization in Children Aged < 5 Years in Northern India. Journal of Infection 68(3): 281-89.
26. Chadha, M. S., Broor, S., Gunasekaran P., Potdar, V. A., Krishnan A., Chawla-Sarkar, M., Biswas D., Abraham, A. M., Jalgaonkar, S. V., Kaur, H., Klimov, A., Lal, R. B., Moen, A., Kant, L, & Mishra, A.C. (2011) Multisite Virological Influenza Surveillance in India: 2004-2008. Influenza and Other Respiratory Viruses 6(3): 196-203.
27. Hirve, S., Chadha, M., Lele, P., Lafond, K., Deoshatwar, A., Sambhudas, S., Juvekar, S., Mounts, A., Dawood, F., Lal R , & Mishra, A. (2012) Performance of Case Definitions Used for Influenza Surveillance among Hospitalized Patients in a Rural Area of India. Bulletin of the World Health Organization 90(11):804-12.
28. Mukherjee, T. R., Chanda S., Mullick S., De., P., Dey-Sarkar, M., & Chawla-Sarkar, M. (2013) Spectrum of Respiratory Viruses Circulating in Eastern India: Prospective Surveillance among Patients with Influenza-like Illness during 2010-2011. Journal of Medical Virology 85(8):1459-465
29. Dangi, T. et al. (2014) Influenza Virus Genotypes Circulating in and around Lucknow, Uttar Pradesh, India, during Post Pandemic Period, August 2010 - September 2012. The Indian Journal of Medical Research 139(3):418–426.
30. Bali, N. K., Ashraf, M., Ahmad F., Khan, U. H., Widdowson, M-A., Lal, R. B., & Koul, P. A. (2012) Knowledge, Attitude, and Practices about the Seasonal Influenza Vaccination among Healthcare Workers in Srinagar, India. Influenza and Other Respiratory Viruses 7(4):540-45.
31. Bhaskar, Emmanuel et al. (2012) Vaccination Rates for Pandemic Influenza among Pregnant Women: An Early Observation from Chennai, South India. Lung India: Official Organ of Indian Chest Society 29(3):232–235.
32. Bhalerao-Gandhi, A., Chhabra, P., Arya, S., & Simmerman J. M. (2015). Influenza and Pregnancy: A Review of Literature from India. Infectious Diseases in Obstetrics and Gynecology 2015
33. Vaccines against Influenza WHO Position Paper. WHO Weekly Epidemiological Record (2012): 461-76.