

Review Article

Current practices in influenza management and barriers to influenza vaccination in Nepal

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Received: 17 October 2025

Revised: 15 November 2025

Accepted: 01 December 2025

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ABSTRACT

Influenza is a viral infection affecting the respiratory tract, resulting in substantial morbidity and mortality. This review article explores the current practices in influenza management and the barriers to vaccination in Nepal. Influenza-associated respiratory deaths account for approximately 2% of all respiratory deaths globally, with higher mortality rates in low to middle income countries (LMICs) like Nepal. Vaccination remains the most effective preventive measure, yet Nepal lacks a formal seasonal influenza vaccination policy, with vaccines available only in the private sector. Current practices emphasize early diagnosis and antiviral treatment within 48 hours of symptom onset, though delayed diagnosis and poor adherence to treatment guidelines are common in Nepal. The article also discusses the vulnerability of specific populations, including children, pregnant women, individuals with chronic medical conditions, the elderly, and healthcare workers. It underscores the need for improved vaccination coverage and policy changes to reduce influenza-related morbidity and mortality in Nepal. Despite the availability of vaccines, certain barriers limit access to vaccination especially in LMICs like Nepal despite established cost effectiveness of influenza vaccination. Targeted vaccination campaigns and public health education are essential to increase awareness and acceptance.

Keywords: Nepal, Influenza, Vaccination, Cost – effectiveness, Respiratory illness

INTRODUCTION

Influenza is a communicable viral infection affecting the upper and lower respiratory tract caused by a wide spectrum of influenza viruses.¹ Globally, Influenza-associated respiratory deaths are estimated around 2% (290,000 to 650,000 deaths) of all respiratory deaths and 14.1% acute respiratory hospitalizations.²⁻⁴ Select populations including children, pregnant women, individuals with chronic medical conditions, elderly and health care workers are more vulnerable to development of influenza related complications and severe illness.³

The influenza complications are seen more in middle- and low-income countries (LMIC) like Nepal as LMIC

countries face more challenges with higher rates of hospitalization and influenza related deaths especially after secondary lower respiratory tract infections.^{5,6}

In 2004, the first influenza outbreak in Nepal was identified at a Bhutanese refugee camp followed by two epidemics in 2004 and 2009.^{7,8} Since then, sporadic outbreaks keep happening around the year. Seasonality of Influenza in Nepal is documented to be in winter however studies have suggested it peaks even during monsoon with the first peak in January–February followed by August–September.⁸

In a retrospective study conducted in Nepal, case fatality rate of the patients infected with Influenza A/Pdm 09 was

22%. In the patients admitted in intensive care unit, the mortality rate was as high as 52.4%. The average duration of stay in the ICU was 6.4 days, while the average time spent on mechanical ventilation was 5.8 days.^{7,8}

Vaccination is the best way to prevent influenza yet there are challenges in effective implementation of recommended vaccination.⁵ Nepal does not have a formal seasonal influenza vaccination policy. Seasonal influenza vaccine is only offered in the private sector.⁵

There is a paucity of studies from Nepal that highlight the need for and importance of influenza vaccination. This article reviews the status of influenza in Nepal and the role of influenza vaccine in reducing the morbidity and mortality associated with influenza in the at-risk population.

METHODS

Independent focus group discussion was chaired by the author along with 9 other experts in the field of pulmonology, medicine, and pediatrics to understand the clinicians' opinions on the current practices in influenza management and barriers to influenza vaccination in Nepal. A literature search using the keywords "Nepal, Influenza, Influenza Vaccination, Co-morbidities, Respiratory Infections, Influenza Management" was conducted. This review explains the importance of influenza vaccination in various populations and the current practices regarding influenza vaccination and management in Nepal.

CURRENT PRACTICES IN MANAGEMENT OF INFLUENZA

The CDC and IDSA guidelines recommend early diagnosis and the early use of antiviral drugs within 48 hours of symptom onset. The mechanism of action for antivirals is inhibition of Neuraminidase which is effective only within 48 hours after which as there is no rationale to use antivirals. The U.S. Food and Drug Administration has approved anti-influenza drugs for use within 48 hours of symptom onset.⁹

The decision to prescribe anti-viral is based on balancing potential benefits, harms, cost, and patient preferences. Both the CDC and the IDSA advise using antiviral therapy for patients who have severe or worsening illness, are at high risk for complications related to influenza, or are hospitalized. The IDSA also recommends that treatment be considered for household contacts of people at high risk of influenza-associated complications.⁹

Diagnosis of influenza in Nepal is often delayed because only a few laboratories are equipped with PCR. Viral swab testing in suspected viral infections is very low in Nepal as compared to other countries (0% vs 15%) leads to a large time lag in treatment initiation.^{10,11} Adherence to

recommendations for treatment with anti-viral is poor in Nepal.¹⁰

Expert opinion

It is almost impossible to start the treatment with antivirals within 24-48 hours in Nepal as testing takes almost a week especially in private set ups, unless the patient is in the ICU. Even in ICUs, it is difficult to get the results within 48 hours. Thus, ICU patients are managed prophylactically with antivirals based on clinical judgement in severe cases while the test results are awaited. Often times, steroids are prescribed for management of severe cases especially when the pathogen has not been isolated.

Efforts to improve and expedite the diagnosis process can be made. Most of the patients are suggested isolation, steam inhalation and antibiotics (if required) and rest. However, in all the scenarios it is better for the patients to be immunized.

CHILDREN

Infants and children are particularly vulnerable to higher rates of infection and complications compared with adults.¹² Around 10% of seasonal influenza cases affect children under the age of 5, leading to approximately 870,000 hospitalizations worldwide.¹³ In infants in rural Nepal, repeated respiratory virus infections are frequent.¹⁴ This results in an average of 20,000 children younger than five being hospitalized due to flu complications each year in Nepal.⁵

The efficacy of influenza vaccine has been estimated to be around 80% in preventing the disease in children.⁵ According to several studies, getting vaccinated against the flu dramatically lowers a child's risk of serious, life-threatening consequences. This risk includes a 75% reduction in severe, life-threatening influenza, a 41% reduction in hospitalizations, and a 50% reduction in ER visits caused by the flu.¹⁵

In a retrospective study conducted between 2011-2020, among 24,148 enrolled children, the pooled Vaccine Effectiveness was 46% across all influenza seasons 32-38% of the secondary household cases from exposure to a sick child could be averted by vaccinating children.^{5,12} Vaccination impedes the transmission of influenza to vulnerable people, family members and older people reducing the mortality of elderly up to 36%.¹⁶

Expert opinion

In Nepal, children have the highest rate of influenza. There is limited published data regarding benefits of influenza vaccination in children for Nepal, but significant clinical improvement has been observed in pediatric population, especially in chronic asthmatic children. Children infected with severe infection with influenza A, may present with severe calf pain. It has been observed that these children

are unimmunized. However, children also have the highest rate of influenza vaccination in Nepal and benefits are experienced during clinical practice as well as by the parents in turn inspiring them to vaccinate themselves along with their children.

PREGNANT WOMEN

Normal pregnancy presents a period of immunological changes which can make pregnant women more susceptible to severe viral infections. The risk of hospitalization from influenza is four times higher during pregnancy.¹⁷ Infants less than 6 months of age are also highly susceptible to influenza infection however influenza vaccination is not approved for the age group.¹⁷

A meta-analysis of 19 studies from 11 countries identified an efficacy of 53% and an effectiveness of 63% of the seasonal inactivated influenza vaccination among pregnant women. A recent multi-country study involving 19,450 pregnant women across four countries and 25 influenza seasons demonstrated that influenza vaccination during pregnancy prevented 40% of influenza cases and influenza-associated hospitalizations.¹⁷

In a pooled analysis of 3 randomized controlled trials conducted in Nepal, Mali, and South Africa, 31% lower incidence rate of severe pneumonia was observed in the influenza vaccine group as compared with the control group in Nepal. The results indicated that maternal influenza immunization may reduce severe pneumonia episodes among infants (2018) reported a 42% (18–59%), reduction in clinic visits for respiratory illness with fever in infants <6 months of age.¹⁸⁻²⁰

Katz et al studied the efficacy of the influenza vaccine in 3600 Nepalese pregnant women and observed that vaccine efficacy did not vary by gestational age at vaccination, making maternal influenza immunization programs much easier to implement in a country like Nepal where women present for antenatal care late in pregnancy.²¹ Clinical trials have shown that while pregnant women report experiencing common adverse events, severe reactions are uncommon highlighting the safety of influenza vaccination during pregnancy. Currently, the majority of evidence focuses on influenza vaccine administered in the second or third trimester.¹⁷

Knowledge gaps regarding the importance of vaccination are a major barrier. A recent meta-analysis revealed that women who received a recommendation from their healthcare provider were 10–12 times more likely to get the recommended vaccines. Conversely, the belief that vaccination could cause harm led to a 78% decrease in the likelihood of getting an influenza vaccine.¹⁷

Expert opinion

In Nepal, the rate of vaccination of pregnant women is fairly low. This is associated with lack of awareness

regarding the importance of vaccination. Pregnant women and their families are highly skeptical towards vaccination during pregnancy and have a strong belief against vaccination. They believe there will be birth abnormalities, miscarriages, and other complications if vaccine is administered.

As a result, most gynecologists leave it on patient's discretion regarding the decision of vaccination and avoid strongly recommending the vaccination. Breast feeding women are recommended to vaccinate themselves against influenza by pediatricians and are well receptive of the same. Thus, if pregnant women are counselled effectively by the gynecologists and made aware of the benefits of vaccination towards the infant; it may lead to increased uptake of vaccination by Nepalese pregnant women.

PATIENTS WITH CO-MORBIDITIES

Individuals with chronic medical conditions account for as many as 80% of all hospital admissions with laboratory-confirmed influenza in adults, and approximately 50% of those in children.^{22,23}

Influenza not only presents with severe illness in patients with existing co-morbidities, but it can also worsen the existing conditions and lead to complications. The CDC has recommended the influenza vaccine in patients with comorbid diseases such as diabetes, cardiovascular disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), elderly with comorbid diseases, immunocompromised patients or patients treated with chemotherapy drugs.²⁴

A randomized phase III trial of a high-dose influenza vaccine in approximately 32,000 subjects showed that it reduced serious cardiorespiratory events by 17.7%, pneumonia events by 39.8%, and congestive heart failure by 24.0%. All of these complications lead to long term hospitalizations which can lead to deconditioning and hamper the speed of recovery and activities of daily living.²⁵

DIABETES

In Diabetics, influenza can delineate blood sugar levels which may also lead to diabetic ketoacidosis.²⁵ Influenza not only increases abnormal glucose levels by 75% but also impacts daily life of diabetic patients, with reduced sleep and physical activity.²⁶ Hyperglycemia can cascade immune responses causing structural changes to the lungs that reduce pulmonary function.²⁶

In a study of 162 hospitalized patients with influenza, the odds of being admitted to an ICU were four times higher for patients with diabetes compared to those without, making this a greater risk than that from cardiac disease. Diabetes patients have a 3.7-fold higher risk of influenza-related healthcare utilization.²⁷ Influenza vaccination has been reported to protect about 3,800 per 100,000 patients with diabetes from risk of death.²⁸

RESPIRATORY DISEASES

Influenza related exacerbations can be observed in patients with chronic respiratory conditions such as COPD and asthma leading to further susceptibility to infection, reduction in lung function, secondary pneumonia, and hospitalization. Around 46% of adults and up to 42% children hospitalized for influenza have been reported to have underlying asthma.²⁵ Bacterial co-infections leading to secondary pneumonia occur in about 11-35% of lab-confirmed influenza patients of all ages.²⁵

Annual influenza vaccination is almost universally recommended in COPD guidelines including American Thoracic Society (ATS); British Thoracic Society (BTS); Global Initiative for Chronic Obstructive Lung Disease (GOLD); and National Institute for Health and Care Excellence (NICE) Guidelines.²⁹⁻³³

In people with chronic lung disease, those who were vaccinated had a 52% reduction in hospitalizations and a 70% reduction in death rate during influenza seasons.³⁴ A meta-analysis of 20 cohort studies on influenza vaccination in older adults found significant benefits: a 56% reduction in respiratory illnesses, a 53% reduction in pneumonia, a 50% reduction in hospitalizations, and a 68% reduction in deaths from all causes during influenza outbreaks.³⁵

CARDIOVASCULAR DISEASES

In patients with cardiovascular conditions, influenza increases the risk of precipitating cardiac events such as Acute Myocardial Infarction (AMI), Stroke and Venous Thromboembolism. Severe illness in an existing diseased individual can lead to myocarditis and heart failure while dehydration and electrolyte imbalances may precipitate acute kidney injury in patients with existing renal impairment.²⁵

A study of 1.9 million hospital admissions for acute myocardial infarction (AMI) found that patients with both AMI and influenza had worse outcomes compared to those with AMI alone. These patients experienced higher rates of in-hospital death, shock, acute respiratory failure, and acute kidney injury.²⁵

Macintyre indicated that influenza vaccine efficacy/effectiveness in preventing cardiac events was roughly equivalent to the one seen with statins antihypertensive treatments, or smoking cessation, suggesting that influenza vaccination should be considered as an integral part of cardiovascular disease management and prevention.^{36,37}

Expert opinion

Respiratory infections are very common with all comorbidities but whether it is influenza is not known due to lack of testing. Specialists in Nepal recommend

influenza vaccination to patients with co-morbidities however in Nepal many patients with co-morbidities visit General physicians. General physicians in Nepal may need to shift their beliefs in the light of vaccine recommendations. Some physicians believe that vaccination is not recommended in patients with comorbidities if they are below 65 years.

ELDERLY

Mortality is higher among elderly people (≥ 65 years old) than among the general population. In a Canadian survey of 5014 adults aged 65 years, 21.5% reported having experienced influenza or influenza-like illness (ILI) in a particular influenza season. Among these patients, 39.3% reported taking more than two weeks to recover, while 3.1% indicated they never fully recovered. Additionally, around 20% experienced health and functional decline during the acute phase of their illness.³⁸

In another study in Canada, 15% of adults 65 years of age experienced catastrophic disability (loss of independence in at least two self-care activities) following hospitalization for influenza.²⁵

Influenza can also raise the risk of falls and fractures, as it often causes unsteady gait or dizziness. ILI hospitalizations are associated with a 13% average increase in the risk of hip fracture hospitalization among long-stay and nursing home residents.²⁵

Influenza vaccination improves general health in elderly people and improves survival.^{39,40} It has been estimated that influenza vaccination could avoid approximately 918,200 influenza cases, 332,000 GP visits, 16,300 hospitalizations and 6,300 deaths annually.

Older adults account for majority of vaccine-preventable influenza cases and deaths and the cost-effectiveness of influenza vaccination in reducing illness, hospitalization and death is well documented in elderly.^{41,42}

Expert opinion

Highest mortality with influenza virus infection is seen in elderly patients. Hence influenza vaccination is strongly recommended. Administering the influenza vaccine before the advent of the seasonal influenza is essential to reduce morbidity and mortality in the elderly population.

HEALTH CARE WORKERS AND HEALTHY ADULTS

Health care workers are 3.4 times more susceptible of developing influenza compared to healthy adults as per a meta-analysis of lab-confirmed flu. When healthcare workers get the flu, it can result in increased absenteeism, disrupting medical services and raising the risk of hospital-acquired infections in other patients, peers or their own family members.⁴³

Another meta-analysis revealed that the overall vaccination rate among healthcare workers was only around 41.7%. In a survey conducted to gauge attitudes of healthcare workers towards vaccination it was found that 88.8% of healthcare workers would undergo mandatory vaccination if offered free of charge and in the workplace. Educational campaigns have shown an impact increasing HCP influenza vaccination from 33% to 61%.³¹⁻⁴⁴

Up to 26% of healthy adults aged 18 to 64 years may be infected with influenza annually, and the associated work absenteeism can result in substantial societal costs. Vaccinating healthy working adults under 65 against influenza can help lower the rates of influenza-like illness (ILI), reduce the number of lost workdays, and decrease physician visits, particularly in years when the vaccine closely matches the circulating viruses.⁴² A systematic review of randomized controlled trials shows that inactivated flu vaccines can prevent 59% of laboratory-confirmed flu cases in healthy adults.⁴³

Common reasons for not getting the influenza vaccine include fear of side effects, needle aversion, cost, and lack of time or convenience. However, well-publicized, free workplace clinics have proven effective in facilitating vaccination by improving access, eliminating costs, and raising employees awareness of the importance of getting vaccinated.⁴⁵

Expert opinion

Vaccination for healthy adults and health care workers is important although they may not be high risk of complications but there is a high risk of transmission from them to their contacts. Vaccination for healthcare workers is generally undertaken at an individual level in Nepal. In private set ups, employers might vaccinate their staff against influenza. Medical professionals and health care workers must vaccinate themselves regularly against influenza.

COST EFFECTIVENESS OF INFLUENZA VACCINATION

Barnighausen suggested that the value of vaccination can be categorized into 'narrow' and 'broad' benefits. Narrow benefits encompass direct health improvements, healthcare cost savings, and protection against productivity losses for vaccine recipients and development of herd immunity. Broad benefits include longer-term improvements in child health, educational outcomes, and macro-economic stability.^{46,47}

Indirect costs make up 88% of the total economic burden of flu in the 18–64 age group, with 75% of direct costs stemming from hospitalizations. Furthermore, flu-related costs rise with age and the presence of underlying health conditions within this age group. Community influenza cases lost 24,300 quality-adjusted life years and caused 2.9 million absences per season.⁴³ In a double-blind,

randomized, placebo-controlled trial conducted during 2 influenza seasons, vaccination reduced Influenza Like Illness, physician visits, and lost workdays by 34%, 42%, and 32%, respectively.⁴²

Expert opinion

Often times people assign budgets to more important vaccinations and leave out influenza vaccination as it is categorized in "optional vaccinations". The term "optional" must be reframed to "recommended" for influenza vaccination and must be propagated amongst all clinicians. Policy makers must play a role in including influenza vaccination in the National Immunization Programs.

CONCLUSION

Influenza significantly impacts Nepal, especially vulnerable groups like children, pregnant women, the elderly, and healthcare workers. Vaccination is the most effective preventive measure, capable of significantly reducing morbidity and mortality. The absence of a formal vaccination policy limits access to vaccination especially in LMICs like Nepal despite established cost effectiveness of influenza vaccination. Targeted vaccination campaigns and public health education are essential to increase awareness and acceptance. Including influenza vaccination in the National Immunization Program will enhance influenza management and provide better protection for Nepal's population against this viral infection.

ACKNOWLEDGEMENTS

The author would like to thank Dr Manjusha Patankar for her assistance in drafting and editing the manuscript. Writing support was funded by Abbott India Limited.

Funding: No funding sources

Conflict of interest: The author received speakers' honorarium from Abbott for participation in focus group discussion

Ethical approval: Not required

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Cite this article as: Chokhani R. Current practices in influenza management and barriers to influenza vaccination in Nepal. *Int J Res Med Sci* 2026;14:305-11.