



## Original Article

## Influenza vaccination in north Indian patients with heart failure



Parvaiz A. Koul\*, Saima Ali, Hyder Mir, Syed J. Ahmad, Shabir Akram Bhat, Muneer A. Bhat

Department of Internal &amp; Pulmonary Medicine, Sher I Kashmir Institute of Medical Sciences, Srinagar, India

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## ABSTRACT

**Background:** No data exists regarding the uptake of influenza vaccination in patients with heart failure (HF) in India. The present study was designed to assess the uptake, knowledge, attitude and practices of the Indian HF patients towards influenza vaccination.

**Methods and results:** Five-hundred patients with acute/chronic HF were approached for a personal interview and responses to an interview recorded in a pre-defined questionnaire depicting their knowledge, attitudes and practice regarding influenza vaccination. Of the 500 approached, 320 (64%, 174 male, age 3–90 years) consented to participate in the survey. Only 7.5% ( $n = 24$ ) knew of influenza as an illness with adverse potential consequences for themselves or their family. Seventeen (5.3%) were aware of potentially serious nature of influenza and 40 (12.5%) knew of the availability of a vaccine against it and its local availability. However only 14 (4.4%) had actually received the vaccine 1–2 times in the past 5 years. Only 21 (6.56%) had been prescribed influenza vaccine by their respective physicians. Reasons for declining vaccination included misperceptions about safety and efficacy of the vaccine. Most of the participants, however, had not been prescribed vaccination at all.

**Conclusions:** Poor influenza vaccination rates in HF mandate intense efforts to improve vaccination rates.

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## 1. Introduction

Influenza is a major cause of morbidity and mortality in high risk populations like those with chronic medical conditions.<sup>1,2</sup> Patients with heart failure (HF) are at a higher risk of hospitalization in the influenza season compared to the non-influenza season<sup>3,4</sup> with winter peaking of the cardiovascular events being attributed to the influenza viral infection as against the earlier attribution to cold weather.<sup>5</sup> Of adults hospitalized during the 2013–2014 influenza season, the most commonly-occurring chronic condition was heart disease, found in 37% of these.<sup>6</sup>

The European Society of Cardiology has recommended influenza vaccination and included it in the treatment guidelines for acute and chronic HF as an essential topic of patient education.<sup>7</sup> Annual vaccination has been recommended by the American Heart Association and the American College of Cardiology since 2006, as a secondary preventive measure for cardiovascular morbidity and all-cause mortality.<sup>7</sup> However the rate of influenza vaccination in patients with cardiovascular disease (CVD) is very low, and even lower in those with long-term disease.<sup>8,9</sup> Only 1 in every 3 adults

with heart disease in USA (34%) received influenza vaccination in 2010, a level of coverage that was essentially unchanged from other below-target rates achieved in 2002.<sup>10</sup> In 2005, vaccination coverage among elderly in USA (65 years old) with heart disease was found to be much higher (71%) than among middle-aged (50–64 years old) and younger (18–49 years old) adults with heart disease (41% and 23%, respectively).<sup>10</sup> A major roadblock to vaccination against influenza in the US is that only about one half of cardiology practices in USA stock influenza vaccine, as opposed to 70% of endocrinology and primary care practices and 90% of pulmonology practices.<sup>11,12</sup>

There is a paucity of literature on the uptake of influenza vaccination in the Indian subcontinent in high risk groups and no data are available on patients with HF. We have previously reported that healthcare workers (HCWs) have a number of misperceptions about influenza vaccination<sup>13</sup> and their prescribing practices to high risk groups like diabetics,<sup>14</sup> pregnant females,<sup>15</sup> and COPD patients<sup>16</sup> are inadequate. The present study has been designed to study the uptake of influenza vaccine among patients with HF, as also assess their knowledge and attitudes towards influenza vaccination.

## 2. Methods

The study was conducted in a tertiary care hospital in north India, where seasonal influenza has been reported with a

\* Corresponding author at: Department of Internal & Pulmonary Medicine, Sher I Kashmir Institute of Medical Sciences, Soura, Srinagar 190011, J&K, India. URL: <http://www.skims.ac.in>

temperate seasonality, from October 2013 to June 2015. Based on an assumed true proportion of 10% of an infinite population, a precision of +0.05 and a confidence level of 0.95, the sample size arrived at was 139. We randomly screened 500 patients diagnosed with HF (acute/chronic), of whom 320 (64%) consented for participation. The participants were interviewed and the responses recorded in a predefined and validated questionnaire. The questionnaire (Table 1) consisted of 21 questions which included demographic information, knowledge, attitudes and practices regarding influenza vaccination and perceptions about influenza. Responses were also requested about vaccination site and information that the participants desired about influenza vaccination and their preferred mode of reaching out to them. The questionnaire was administered by one of the investigators who are working in the Influenza laboratory of the hospital and apart from having participated in similar surveys previously were trained specifically for the study. They spoke the same dialect as that of the participating patients. The responses recorded were analyzed using descriptive statistics of the recorded variables (Statistical Package for Social Sciences, version 17). Informed consent was obtained from all participants and the survey was approved by the Institute Ethics Committee.

### 3. Results

The 320 consenting participants consisted of 146 male and 174 female patients, either currently admitted with HF or seen during a post-discharge follow-up visit. The age of the patients ranged from 3 years to 90 years; 60% ( $n = 191$ ) being  $\geq 60$  years. Only 3 (0.93%) patients were younger than 18 years of age whereas 26 (8.12%) belonged to the 18–39 year age group and 100 (31.25%) to the 40–59 year group. Two-hundred forty-six patients were from rural setting whereas the rest were from urban setting. Various co-morbidities included COPD ( $n = 87$ , 27.2%), hypertension ( $n = 54$ , 16.9%), community-acquired pneumonia (CAP) ( $n = 35$ , 10.9%), type 2 diabetes mellitus ( $n = 39$ , 12.2%), and dilated cardiomyopathy ( $n = 13$ , 4.1%).

Only 7.5% ( $n = 24$ ) of the participants considered influenza as an illness with adverse potential consequences for themselves or their family. Seventeen (5.3%) were aware of its potentially serious nature and 40 (12.5%) knew of the availability of a vaccine against influenza and its local availability. However only 14 (4.4%) had received the vaccine 1–2 times in the past 5 years, >70% of those vaccinated being >60 years of age (Table 2). None of the participants aged <40 years had received the vaccine twenty-one (6.56%) of the participants had been prescribed influenza vaccine by their respective physicians but only 14 complied receiving the vaccine in hospitals 4(28.57%), private clinics 6 (42.85%) or through family doctors 4 (28.57%). The 7 declining vaccination despite prescription possessed concerns about vaccine safety, believing it to be capable of causing immune and other system disorders. Others who did not receive vaccination were not aware of the seriousness of influenza and some responded that they did not have time for vaccination. However, most ( $n = 292$ ) of the patients had not been advised vaccination by their respective physicians.

The participants expressed a desire for convenient dissemination of information regarding various aspects of influenza vaccination including current year's vaccine, difference between common cold and flu, safety and adverse effects of vaccination. Most of them desired that the information be circulated through various means of technology ranging from radio (41.87%), SMS via mobile phones (26.25%), print newsletter (24.68%) or electronic mail (7.18%).

**Table 1**  
Questionnaire for Survey of Influenza vaccination in CCF.

1. Patient identifier: #.....
2. Residence:..... (R/U)
3. Age :.....yrs
4. Sex : M/F
5. Occupation :.....
6. Monthly income from all sources.....
7. Educational status:
  - a. Uneducated
  - b. Primary level education
  - c. Secondary level education
  - d. Graduate level education
  - e. Professional level
8. Diagnosis: .....
9. Duration of Disease: .....
10. Number of previous hospitalizations: .....
11. Do you have knowledge of potential health consequences of influenza for yourself & your family? Yes / No
12. Do you consider influenza considered as a potentially severe disease? Yes / No
13. Do you know of a vaccine is available? Yes / No
14. Has your doctor told you a requirement of vaccine? Yes / No
15. Have you ever had influenza vaccine in last 5 years? Yes / No
16. If you have received influenza-vaccine before, where so you usually obtain the shot?
  - a. Family Doctor
  - b. Hospital
  - c. Private Clinic
  - d. Other
17. If a doctor told you to get vaccinated. Why did you not get the shot?
  - a. Didn't have time for vaccine.
  - b. Vaccine weakens immune system.
  - c. Vaccines are made & driven for profit.
  - d. I don't get flu.
  - e. I don't think influenza is a serious illness.
  - f. I can't afford the vaccine.
  - g. Others (specify).....
18. Do you consider influenza vaccine to be safe?.....Yes/No
19. If you consider the vaccine to be unsafe, why do you consider it to be so:
  - a. It can harm my immune system
  - b. It can worsen my disease
  - c. It can harm my joints
  - d. A physician told me that it is unsafe
  - e. I know of patient who got sick after vaccination.
  - f. Other (specify).....
20. What type of information would be the most important for you to receive about the influenza prevent on program?
  - a. Details regarding current year's vaccine.
  - b. Difference between common cold and flu
  - c. Influenza outbreak information
  - d. Information about effectiveness of vaccine
  - e. Commonly expected side effects of vaccine
  - f. Information about safety of vaccine
  - g. Information about seriousness of influenza
  - h. Other (Please Specify).....
21. What is the best way to read you with information about influenza vaccine?
  - a. E-mail
  - b. Newsletter
  - c. Mobile phones
  - d. Any Other (Please Specify).....

### 4. Discussion

Our data suggest a poor vaccination uptake in Indian patients with HF. The study, to the best of our knowledge, is the first study that addresses this aspect of patients with HF in the Indian subcontinent. The practices of the physicians and the patients across other areas of the subcontinent need to be studied in order to ascertain if the data are extrapolatable to other areas of the subcontinent.

Most of the vaccinated participants in the current study were aged 60 years or above (Table 2). A higher vaccination uptake has

**Table 2**

Distribution of the participants in various age groups and the vaccination rates. Columns 2 and 3 depict number and percentages of the total vaccinated and unvaccinated participants whereas column 4 depicted the number and percentage rates in different age groups.

Age group	Vaccinated (n = 14) N (%)	Non-vaccinated (n = 306) N (%)	Total vaccinated of the age group N (%)
<18 years	0 (0)	3 (1)	0 (0)
18–39 years	0 (0)	26 (8.5)	0 (0)
40–59 years	4 (28.6)	96 (31.4)	4 (4)
≥60 years	10 (71.4)	181 (59.2)	10 (5.2)

previously been reported in this age group by Hak et al.<sup>17</sup> and Bittner et al.<sup>18</sup> This age group constitutes a high risk group for complications related to influenza and is a high priority for vaccination. Additionally, frequent presence of other comorbidities in them encompasses them as a high-risk group for influenza, independent of the presence of HF. The effects of socioeconomic factors and educational status could not be ascertained as the number of recipients of vaccination was very low and most (n = 10) of them were aged >60 years and were uneducated.

The benefits of influenza vaccination in CVD are not clearly defined. In a recent Cochrane review of 8 studies involving 12,029 participants receiving at least one vaccination or control treatment, the authors concluded that the data did not provide enough information to show the effectiveness of influenza vaccination in the primary prevention of fatal or non-fatal cardiovascular events. However, in patients with established CVD, evidence suggested that influenza vaccination may reduce cardiovascular mortality and combined cardiovascular events.<sup>19</sup> In another recent study, a lower risk of hospitalization for acute coronary syndrome (ACS) was observed among patient with COPD receiving influenza vaccination. Similar protective effect regardless of influenza seasonality was observed in both sexes and all age groups.<sup>20</sup> In yet another prospective population-based cohort involving 1964 participants with acute HF, influenza vaccination was associated with improved survival in acute HF.<sup>21</sup> The benefits of vaccination against influenza are not restricted to prevention of decompensation of cardiac failure due to respiratory infections. Vaccination has been related to other events, such as the primary and secondary prevention of coronary events, reduction of cerebrovascular accidents, reduced hospitalizations and costs for other diseases, especially among the elderly.<sup>17,22,23</sup>

The mechanisms underlying the cardiovascular protective effect of influenza vaccine are poorly understood. One current hypothesis states that the inflammatory response of the body to influenza viral infection produces autoantibodies to modified low-density lipoprotein, thus developing and progressing atherosclerotic vascular injury, while another hypothesis postulates the initiation and perpetuation of inflammatory response by activation of antigen presenting cells by local colonization of vessel wall.<sup>24</sup> Using informational spectrum method, Velijkovic et al. identified bradykinin 2 receptor (BKB2R) as a principal host protein that could mediate molecular processes underlying the cardioprotective effect of influenza vaccines. They suggested that some antibodies elicited by influenza vaccines act as agonists, which activate a BKB2R-associated signalling pathway contributing to the protection against CVD.<sup>21</sup> Patients with HF mount a lower antibody response upon vaccination and the antibody titres to influenza A vaccine strains wane to below seroprotective levels in HF patients compared with healthy controls, despite similar rates of initial seroprotection and seroconversion. These findings suggest that HF patients may remain at increased risk for influenza infection despite annual vaccination<sup>25</sup> and cautiously might

suggest the possible role of high dose flu vaccine or a twice annually schedule of vaccination. Both of these approaches need to be studied for comparative immunogenicity so that recommendations can be based on more robust scientific evidence.

Our study is limited by the fact that it was conducted in a tertiary care setting and the results may not be possible to be extrapolated to other primary and secondary care settings. However we believe that the level of awareness and uptake of vaccination is likely to be even lower in those settings. Nonetheless further studies in those settings would give a complete picture and need to be conducted on priority. With its diverse geography and socio-cultural practices, the knowledge, attitudes and practices regarding vaccination could exhibit significant dispersion which needs study. Another limitation of the study is that the knowledge, attitudes and practices of the caregivers was not assessed. However our recent data suggest that there is inadequate knowledge about influenza vaccination among healthcare workers, there are misperceptions about safety and there is a disconnect between perceptions and practice.<sup>13</sup>

In conclusion, vaccination uptake in Indian patients with HF is poor, rooted primarily in inadequate prescription practices by healthcare providers who thus require sensitization regarding vaccination efficacy and safety. Measures aimed at increasing the uptake need urgently to be put in place.

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## Author contribution

SA, HM, SAK, SJA, MAB participated in data acquisition, analysis and interpretation. PAK designed and supervised the survey and wrote the first draft of the manuscript. All contributed to the final write-up of the manuscript and have approved the same for submission.

## Conflicts of interest

The authors have none to declare.

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