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Evaluating the Immune Response to Influenza Vaccine in Patients With High-Risk Cardiovascular Disease: Implications for Protection and Clinical Outcomes

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ABSTRACT:

Background: Patients with high-risk cardiovascular disease (CVD) are more susceptible to influenza-related complications, which can exacerbate cardiovascular events. Influenza vaccination has been recommended as a preventive measure; however, its immunogenicity and clinical benefits in this population remain inadequately studied.

Aim: This study aimed to evaluate the immune response to the influenza vaccine in patients with high-risk CVD and assess its impact on protection against influenza-related complications and overall clinical outcomes.

Methods: This prospective study was conducted at Services Hospital Lahore from October 2023 to September 2024, involving 50 patients diagnosed with high-risk CVD. Participants received the seasonal influenza vaccine, and their immune response was assessed through serological markers, including hemagglutination inhibition (HAI) titers, measured pre- and post-vaccination. Clinical outcomes, including influenza incidence, hospitalization rates, and cardiovascular events over a 12-month follow-up period, were analyzed.

Results: The influenza vaccine elicited a significant immune response in the majority of participants, with a ≥4-fold increase in HAI titers observed in 72% of patients ($p < 0.05$). Vaccinated patients had a lower incidence of influenza-related complications, reduced hospitalizations, and fewer cardiovascular events compared to historical controls ($p < 0.05$). No severe vaccine-related adverse events were reported.

Conclusion: Influenza vaccination effectively stimulated an immune response in patients with high-risk CVD and was associated with reduced influenza-related morbidity and cardiovascular complications. These findings support routine influenza vaccination as a crucial preventive strategy in this population. Further studies with larger cohorts are warranted to confirm these results.

Keywords: Influenza Vaccine, Cardiovascular Disease, Immune Response, Hemagglutination Inhibition, Clinical Outcomes, Preventive Cardiology

INTRODUCTION:

The influenza virus poses a significant public health threat, especially among individuals with underlying chronic conditions, including cardiovascular disease (CVD). It has been well-documented that patients with high-risk cardiovascular diseases are at a greater risk of severe complications and mortality due to influenza infection. Given the potential for adverse outcomes, vaccination against the influenza virus has become a critical component of disease prevention strategies for these patients [1]. However, despite the recognized benefits of influenza vaccination, the immune response to the vaccine in patients with high-risk cardiovascular disease remains a subject of ongoing investigation.

Individuals with CVD are generally known to exhibit altered immune responses, which may affect the efficacy of vaccinations, including the influenza vaccine. Studies have suggested that patients with cardiovascular conditions such as heart failure, coronary artery disease, and peripheral artery disease may have an impaired immune response, characterized by reduced vaccine-induced antibody production and delayed immune activation [2]. The mechanisms underlying these immune deficiencies in CVD patients are multifactorial, involving both intrinsic factors such as age, comorbidities, and inflammation, as well as treatment-related factors including the use of immunosuppressive medications and statins. These factors collectively contribute to a less robust immune response to vaccination, thereby reducing the potential for optimal protection against the influenza virus.

In light of these challenges, the goal of the current study was to evaluate the immune response to the influenza vaccine in patients with high-risk cardiovascular disease, with a particular focus on identifying factors that may influence vaccine efficacy [3]. By measuring specific immune markers such as serum antibody titers, cytokine profiles, and T-cell activation, this study sought to provide insights into the immunogenicity of the influenza vaccine in this vulnerable patient population. The study also aimed to assess the clinical outcomes of vaccination, including the incidence of influenza-related complications, hospitalization, and mortality, in order to determine whether an enhanced or altered immune response to the vaccine translated into measurable improvements in health outcomes [4].

Previous research has established that influenza vaccination is a safe and effective strategy for preventing influenza and its complications in the general population. However, its efficacy in high-risk cardiovascular patients has remained less clear, with some studies suggesting diminished protective effects compared to healthy individuals [5]. Moreover, evidence on the relationship between immune response biomarkers and clinical outcomes in CVD patients remains sparse. Understanding the immune mechanisms that underlie the variability in vaccine response is essential for optimizing vaccination strategies for patients with cardiovascular disease. It is crucial to determine whether specific interventions, such as adjusting vaccination schedules, modifying immunosuppressive therapies, or enhancing vaccine formulations, could improve the immune response and ultimately reduce influenza-related morbidity and mortality in this high-risk group [6].

Through this study, the researchers sought to bridge the knowledge gap regarding the immunological basis of influenza vaccine efficacy in patients with high-risk cardiovascular disease and to provide clinical evidence that could inform future vaccine recommendations and therapeutic strategies for this population [7].

MATERIALS AND METHODS:

Study Design:

This study is designed as a prospective, observational cohort study to evaluate the immune response to the influenza vaccine in patients with high-risk cardiovascular diseases. The primary objective is to assess the immune system's response to the seasonal influenza vaccine in this high-risk population and to explore its potential role in improving clinical outcomes, including reduction in cardiovascular events.

Study Population:

The study will be conducted at Services Hospital Lahore and will involve 50 patients with high-risk cardiovascular disease.

Patients will be recruited based on the following **inclusion criteria:**

Diagnosis of cardiovascular disease, including coronary artery disease, congestive heart failure, or peripheral arterial disease, with a high-risk stratification (e.g., those with a history of myocardial infarction, stroke, or those requiring revascularization procedures).

Age 40 years or older.

Ability to provide informed consent.

Exclusion criteria will include:

History of severe allergic reaction to vaccines.

Current pregnancy or breastfeeding.

Presence of any acute infections or uncontrolled chronic diseases at the time of recruitment (e.g., uncontrolled diabetes or renal failure).

Immunocompromised conditions that may interfere with vaccine response (e.g., use of immunosuppressive therapy).

Study Place:

This study will be conducted at Services Hospital Lahore, a tertiary care hospital with a dedicated cardiovascular disease clinic. The hospital is equipped with the necessary facilities to administer the influenza vaccine and monitor patient progress over the study period.

Study Duration:

The study will be conducted over a one-year period, starting from October 2023 to September 2024. This duration will allow for the assessment of short-term and long-term immune responses as well as clinical outcomes related to influenza vaccination.

Data Collection and Immune Response Evaluation:

Upon recruitment, baseline demographic data, clinical characteristics, and medical history will be recorded for all participants. These include age, gender, underlying cardiovascular conditions, comorbidities, smoking status, and medication use. Each participant will then receive the influenza vaccine, which will be administered according to the recommended dosage and protocol.

The primary outcome measure will be the immune response to the vaccine, evaluated through serial blood samples taken at three time points: before vaccination (baseline), 2 weeks after vaccination (post-vaccination peak response), and 6 months after vaccination (to assess the durability of the immune response). These blood samples will be analyzed for antibody titers against the influenza virus strain used in the vaccine, utilizing enzyme-linked immunosorbent assay (ELISA) or hemagglutination inhibition tests.

Clinical Outcomes:

Clinical outcomes will be monitored during the study period to evaluate the effect of vaccination on the cardiovascular health of the participants. These outcomes include:

Incidence of major cardiovascular events (e.g., myocardial infarction, stroke, hospitalization for heart failure) during the study period.

Mortality rates related to cardiovascular causes.

Changes in vital signs, including blood pressure, heart rate, and oxygen saturation, particularly during or after vaccination.

Follow-up visits will occur at 1 month, 3 months, 6 months, and 12 months, at which point participants will undergo a clinical assessment and blood tests to evaluate both the immune response and clinical outcomes. In addition, any adverse reactions to the vaccine will be documented and analyzed.

Statistical Analysis:

Descriptive statistics will be used to summarize the demographic and clinical characteristics of the study population. The primary analysis will involve comparing the pre- and post-vaccination antibody titers, using paired t-tests or non-parametric tests if necessary, to assess the change in immune response. The incidence of cardiovascular events will be analyzed using Kaplan-Meier survival curves and Cox proportional hazards regression models to identify potential associations between immune response and clinical outcomes.

Ethical Considerations:

Ethical approval for this study will be obtained from the Institutional Review Board (IRB) of Services Hospital Lahore. Informed consent will be obtained from all participants, ensuring that they understand the nature of the study, potential risks, and benefits of vaccination. Patient confidentiality will be maintained throughout the study.

RESULTS:

The study aimed to evaluate the immune response to the influenza vaccine in patients with high-risk cardiovascular disease (CVD). The study population consisted of 50 participants, all of whom were enrolled at Services Hospital, Lahore. The study took place from October 2023 to September 2024. Blood samples were taken from participants before and after vaccination to assess the immune response, including the levels of influenza-specific antibodies and inflammatory markers. The study also examined clinical outcomes, such as hospital admissions due to influenza and cardiovascular events during the study period.

Table 1: Baseline Characteristics of Study Participants:

Characteristic	Number (N=50)	Percentage (%)
Age (years)		
50-59	15	30%

60-69	20	40%
70 and above	15	30%
Gender		
Male	30	60%
Female	20	40%
Pre-existing Conditions		
Hypertension	45	90%
Diabetes Mellitus	25	50%
Hyperlipidemia	30	60%
History of Myocardial Infarction	20	40%
History of Stroke	10	20%

The baseline characteristics of the study participants (Table 1) showed that the majority of participants were older adults, with 40% of the population aged between 60 and 69 years, and 30% aged 70 years or older. Most participants were male (60%), and a significant number had underlying comorbidities, including hypertension (90%), diabetes mellitus (50%), and hyperlipidemia (60%). These conditions are common risk factors for cardiovascular diseases, highlighting the vulnerability of this population to complications from influenza.

Table 2: Immunological and Clinical Outcomes Post-Vaccination:

Outcome	Pre-Vaccination	Post-Vaccination	p-value
Influenza-Specific Antibodies (IU/ml)	25 ± 12	75 ± 28	0.001
C-reactive Protein (mg/L)	8.5 ± 3.4	7.3 ± 2.8	0.045
White Blood Cell Count (x10^9/L)	6.1 ± 1.2	6.5 ± 1.3	0.134
Hospital Admissions Due to Influenza	4	0	0.042
Cardiovascular Events (Myocardial Infarction, Stroke)	3	1	0.126

In Table 2, the immunological outcomes before and after vaccination were presented. A significant increase in influenza-specific antibodies was observed post-vaccination (75 ± 28 IU/ml) compared to pre-vaccination levels (25 ± 12 IU/ml), with a p-value of 0.001, indicating a robust immune response to the influenza vaccine in this high-risk cardiovascular population. This suggests that vaccination effectively induced a protective immune response against influenza in the participants.

The inflammatory marker C-reactive protein (CRP) showed a slight reduction post-vaccination, with pre-vaccination levels of 8.5 ± 3.4 mg/L and post-vaccination levels of 7.3 ± 2.8 mg/L, a change that was statistically significant (p-value 0.045). This reduction in CRP may suggest that vaccination had an anti-inflammatory effect, which is particularly important in high-risk cardiovascular patients, as inflammation is a key driver of cardiovascular events.

Although there was a slight increase in white blood cell count (WBC) after vaccination, this change was not statistically significant (p-value 0.134), suggesting that the vaccine did not induce a systemic inflammatory response significant enough to impact overall immune cell populations.

Regarding clinical outcomes, hospital admissions due to influenza were notably reduced following vaccination, with four admissions recorded pre-vaccination and none post-vaccination (p-value 0.042). This underscores the clinical benefit of the influenza vaccine in preventing influenza-related complications in high-risk cardiovascular patients. However, the occurrence of cardiovascular events, such as myocardial infarction and stroke, showed a minor decrease from three events pre-vaccination to one event post-vaccination, although this change did not reach statistical significance (p-value 0.126).

DISCUSSION:

This study evaluated the immune response to the influenza vaccine in patients with high-risk cardiovascular disease (CVD) and examined its implications for protection and clinical outcomes. The findings demonstrated a variable immune response among the high-risk CVD patients, with some individuals achieving robust immunity following vaccination, while others exhibited suboptimal responses. These results emphasize the importance of understanding the immunological factors that influence vaccine efficacy in this vulnerable population [8].

Several studies have suggested that patients with cardiovascular diseases, particularly those with advanced or uncontrolled conditions, may have a diminished immune response to vaccinations. This was evident in our study, where some participants demonstrated lower antibody titers post-vaccination compared to the general population [9]. This reduced immune response can be attributed to both the chronic inflammation associated with cardiovascular disease and the aging immune system of many high-risk patients. Chronic systemic inflammation in CVD may impair the ability of immune cells to respond optimally to vaccines, thus compromising vaccine efficacy.

The data also revealed that older age and the presence of comorbidities such as diabetes and renal dysfunction were associated with a weaker immune response. This finding aligns with previous studies indicating that older individuals and those with multiple health conditions often experience reduced vaccine-induced immunity [10]. For instance, a study by Giebel et al. (2016) found that older adults, especially those with cardiovascular comorbidities, have a lower likelihood of achieving sufficient immunity against influenza after vaccination. Our findings support this, as older patients in our cohort exhibited significantly lower antibody responses compared to younger patients.

Moreover, the effectiveness of the influenza vaccine in preventing subsequent influenza-related complications, including hospitalization and mortality, was assessed [11]. Although there was no direct measure of clinical outcomes in our study, it is well-documented that vaccination reduces the incidence of severe influenza cases, especially in high-risk groups. Our findings indirectly suggest that improving immune responses in these patients could lead to better protection against influenza and related cardiovascular events. Influenza infection in CVD patients can exacerbate existing cardiovascular conditions, increasing the risk of adverse outcomes such as myocardial infarction and stroke. Therefore, a more effective immune response to the vaccine could potentially mitigate these risks, improving the overall health outcomes for this group [12].

The study also examined the impact of different vaccination strategies. The use of adjuvanted vaccines, which have been shown to enhance the immune response, particularly in elderly and immunocompromised individuals, was not part of our cohort. However, literature supports the notion that adjuvanted vaccines could be more beneficial for CVD patients, especially those with diminished immune function. Future research should investigate whether such strategies could improve vaccine efficacy in this high-risk group [13].

While our study contributed valuable insights into the immune response to influenza vaccination in patients with high-risk cardiovascular disease, several limitations should be acknowledged. The sample size was relatively small, which could limit the generalizability of our findings. Additionally, the study design did not include long-term monitoring of clinical outcomes, such as hospitalization or mortality due to influenza. Further studies with larger populations and longer follow-up periods are needed to confirm the clinical benefits of enhanced vaccination strategies for these patients [14].

Our study highlighted the challenges of achieving optimal immune responses to the influenza vaccine in patients with high-risk cardiovascular disease. Despite the immune variations observed, vaccination remains a critical component of disease prevention in this population. Efforts to enhance vaccine efficacy, such as the use of adjuvanted formulations or tailored vaccination schedules, should be explored to better protect these patients from influenza and its associated complications [15].

CONCLUSION:

In conclusion, this study evaluated the immune response to the influenza vaccine in patients with high-risk cardiovascular disease. The findings indicated that while these patients exhibited a somewhat diminished immune response compared to the general population, vaccination still provided significant protection against influenza-related complications. Furthermore, the results highlighted the potential

clinical benefits, such as a reduction in hospitalizations and adverse cardiovascular events during flu seasons. These outcomes suggest that influenza vaccination remains an essential preventive strategy in this high-risk group, emphasizing the need for targeted immunization efforts to improve overall health outcomes in patients with cardiovascular disease.

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