RESEARCH PAPER

Predictive Biomarkers for Mortality Risk Assessment in Geriatric Individuals Following COVID-19 Booster Vaccination: A District-Level Study from Assam, India

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ABSTRACT

Cardiovascular and respiratory diseases remain major contributors to morbidity and mortality among elderly individuals due to age-related physiological decline, multimorbidity, and reduced immune responsiveness. Although COVID-19 booster vaccination has demonstrated a favorable safety profile globally, evidence regarding biomarker-based assessment of post-vaccination cardiopulmonary outcomes among geriatric populations in Northeast India remains limited. The present prospective cohort study evaluated predictive biomarkers associated with cardiovascular and respiratory events following COVID-19 booster vaccination among elderly individuals in selected districts of Assam, including Dhubri, Goalpara, Barpeta, and Bongaigaon. A total of 400 participants aged ≥60 years were followed for 12 months using active telephonic surveillance and verification through hospital records to identify incident clinical events. Organ-specific biomarkers, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP), peripheral oxygen saturation (SpO_2), serum creatinine, and blood urea nitrogen (BUN), were assessed at baseline and follow-up to evaluate physiological responses after vaccination. During the follow-up period, 24 cardiovascular events and 32 respiratory events were recorded, corresponding to cumulative incidences of 6% and 8%, respectively, with higher event rates observed among participants aged ≥71 years and those with pre-existing comorbidities. Mild but statistically significant elevations in hepatic enzymes and CRP levels were observed; however, these remained within normal clinical limits. No significant changes were detected in renal function markers or oxygen saturation levels. Overall, the findings indicate that COVID-19 booster vaccination was well tolerated among geriatric individuals. Biomarker-guided monitoring may facilitate early identification of high-risk individuals and support evidence-based post-vaccination surveillance strategies in resource-limited regional healthcare settings such as Northeast India.

KEYWORDS:COVID-19 booster vaccination, Geriatric population, Cardiovascular events, Respiratory complications, Predictive biomarkers. Northeast India

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INTRODUCTION

Cardiovascular diseases (CVDs) and respiratory disorders are still the primary causes of morbidity and mortality globally, representing a considerable burden of health-related complications in elderly populations. Advancing age leads to progressive structural and functional decline of cardiovascular and pulmonary systems, such as lower elasticity of the vasculature, impaired myocardial reserve, decreased lung compliance, and reduced immune responsiveness [1][2]. Combined with chronic comorbid conditions such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), ischemic heart disease and chronic kidney disease that increase vulnerability for adverse clinical outcome.These physiological dysregulations are compounded leading to poorer long-term outcomes. Moreover, elderly patients often have whispers of frailty, multimorbidity and polypharmacy with reduced physiological reserve and are at increased risk for acute medical events as well as risk of death [3][4].

The coronavirus disease 2019 (COVID-19) pandemic significantly burdened elderly populations, who faced disproportionately higher rates of hospitalization, severity of disease, and mortality than younger individuals. Old age and pre-existing cardiopulmonary conditions were identified as consistent major predictors for deleterious clinical outcomes during the pandemic. Consequently, vaccination strategies were soon implemented in many places around the world to

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mitigate infection-related morbidity and mortality. In India, booster doses of vaccines like Covishield and Covaxin were rolled out to boost immune protection for the predominant immunosuppressed populations including elderly individuals and patients with chronic comorbidities [5][6].

Despite favorable safety profiles and robust immunogenic responses following COVID-19 booster vaccination in the general population, concerns aboutvaccine-induced immune responses interacting with pre-existing comorbid pathology in older individuals persists. Notably, older individuals with pre-existing cardiovascular and respiratory diseases may have different physiological responses to vaccination owing age-associated immunological dysregulation and compromised organ functionality. As a result, systematic assessment of clinical outcomes after vaccination including risk factors to such events in this high-risk population are important for proper monitoring around vaccine safety and informing public health strategies [7][8].Recognizing predictive risk factors related to cardiovascular and respiratory events less than a week after booster vaccination is an invaluable step toward fortifying geriatric health care provisioning. In this regard, analyzing organ-specific biomarkers like the liver function enzymes, inflammatory markers such as cytokines, and oxygen saturation levels and renal function parameters could provide an in-depth view of physiological responses post-vaccination [9][10]. Monitoring of biomarker levels helps to detect adverse clinical events early and can aid the formulation of predictive models for mortality risk stratification in older adults. These predictive approaches also have increased relevance in resource-constrained healthcare environments, guiding targeted clinical surveillance as well as intervention strategies among individuals with an elevated disease risk [11][12].

Although data on the safety of COVID-19 vaccines are there globally now, evidence for biomarker-based risk assessment of cardiovascular and respiratory outcomes post-booster vaccination among geriatric population in Northeast India remain scanty [13]. The epidemiological patterns may also differ at the local context, coupled with variation in healthcare access and availability; therefore, localized studies are essential for generating context-specific clinical evidence. The diverse socio-demographic characteristics and range of healthcare infrastructure across Assam provides a relevant milieu for assessing post-vaccination clinical events among older adults [14].

Hence, the current prospective cohort study was performed among geriatric individuals vaccinated with the COVID-19 booster dose in selected districts of Assam-Dhubri, Goalpara, Barpeta and Bongaigaon to understand predictive biomarkers upholding mortality risk. Additionally, the study aimed to assess the frequency of post-vaccination clinical events during one-month to up to one year period following vaccination with booster doses and its relationship with cardiovascular and respiratory adverse events; this allowed identification of associated risk factors. We also aimed to explore differences in selected organ-specific biomarkers after vaccination. The study also aimed to establish a model of prediction for individuals at high risk of developing severe diseases. These results are anticipated to inform geriatric vaccination strategies through a more evidence-based approach and aid the development of biomarker-driven risk prediction models that optimize clinical decision-making for prioritized immunization in elderly populations living in resource-limited regional healthcare environments.

MATERIALS AND METHODS

Study Design

A prospective cohort study design was implemented to address cardiovascular and respiratory risk factors in geriatric individual adults receiving COVID-19 booster vaccination. Participants were enrolled at booster vaccination time and followed longitudinally for up to 12 months to record incident cardiovascular and respiratory outcomes [15].

Study Setting

The base line survey was carried out during October, 2020 to December, 2020 among selected districts of Assam i.e., Dhubri, Goalpara, Barpeta and Bongaigaon. Participants were recruited from government hospitals, community hospitals, medical colleges, NABL accredited laboratories and government vaccination centres [16].

Study Population

We performed the analysis in geriatric patients aged 60 years and above, who received the booster dose after completion of their primary vaccination schedule [17].

Collection of Baseline Information

Structured data collection format was developed at the begining to assure standard and complete clinical records. For all geriatric participants enrolled, demographic characteristics, an extensive medical history, comorbidities, medication history and date of COVID-19 booster vaccination were recorded. Wherever possible, previously obtained laboratory investigation reports were reviewed and regarded as baseline reference values for organ specific biomarker assessment. These baseline measurements enabled future comparison with post-vaccination clinical results and biomarker changes at follow-up assessment [18].

Operational Definitions

To ensure consistent categorization of study variables and clinical outcomes for all participants included in the prospective cohort study, we established operational definitions [19].

Geriatric Population
Geriatric subjects were individual aged ≥60 years who received a booster dose of COVID-19 vaccine following the completion of one primary vaccination schedule [20].

COVID-19 Booster Dose
A COVID-19 booster dose was defined as any supplementary vaccine dose received after completion of the primary series with either Covishield or Covaxin according to national immunization guidelines.

Cardiovascular Events
Cardiovascular events were defined as the occurrence of any clinically confirmed conditions during follow-up:
• Acute coronary syndrome
• Myocardial infarction, supported by electrocardiographic findings and/or increased levels of cardiac troponin
• New-onset heart failure requiring hospitalization
• Arrhythmia requiring therapeutic intervention
These criteria allowed consistent identification of clinically meaningful cardiovascular complications in participants.

Respiratory Events
Respiratory events were defined as the development of any of the following conditions requiring clinical management:
• Acute exacerbation of chronic obstructive pulmonary disease (COPD) needing treatment
• Pneumonia confirmed clinically and/or radiologically
• Severe respiratory failure necessitating supplemental oxygen or hospitalization
These definitions enabled uniform categorization of respiratory complications upon booster immunization in the participating geriatric population.

Sample Size
A total sample size of approximately 500 geriatric individuals receiving COVID-19 booster vaccination participating in the study was selected and included based on feasibility considerations as well as the number of eligible subjects across potentially selected districts of Assam to evaluate biomarkers variation while assessing risk factors associated with cardiovascular and respiratory events and mortality outcome following infectious episodes [21].

Collection of Baseline Information
It is a longitudinal study and data of baseline information were collected by a structured, pre-validated case report form that allowed uniform, reliable and complete clinical documentation in all enrolled participants [22]. Demographic information regarding age and gender, history of acute illness preceding admission, was recorded (including known pre-existing comorbid conditions and medication profiles). Data on lifestyle-related risk factors including smoking status and alcohol consumption were also recorded.
Baseline measurements of vital clinical parameters such as blood pressure, body mass index (BMI), and heart rate were conducted through standard clinical procedures. Information on COVID-19 vaccination (type of vaccine, date of booster dose and history of SARS-CoV-2 infection) was recorded systematically. Pre-vaccination clinical status was defined by baseline cardiac and respiratory symptoms recorded at the time of enrollment.
When available, previous laboratory investigation reports were reviewed and utilized as baseline reference values for organ-specific biomarker assessment. Such baseline parameters formed valuable reference shares for comparing post-vaccination clinical events and biomarker changes at follow-up assessment, allowing risk stratification and predictive biomarker exploration in the geriatric study sample.

Inclusion Criteria
Study participants were included if they met the following criteria [23]:
• Were aged ≥60 years
• Had received or were due to receive a booster dose of COVID-19
• Provided informed consent

Exclusion Criteria
Participants were excluded if they [24]:
- Had active acute cardiovascular or respiratory illness at enrollment
- Terminal illness life expectancy <6 months
- Required hospitalization for severe illness unrelated to the speech
- Had incomplete primary vaccination
- Personal history of severe vaccine allergy
- Prolonged immunosuppressive therapy for autoimmune disorders

Sampling Strategy
The study utilized a stratified random sampling method with proportional allocation to guarantee that all age groups of the geriatric population were represented accordingly. The study population was sub-stratified based on age categories, that is, 60–70 years and ≥71 years, due to their potential differences in clinical vulnerability and physiological responses post COVID-19 booster vaccination. For instance, individuals aged 60–70 years formed about 85% of the study sample, and those ≥71 years made up 15% of total sample [25].
The planned sample size of 500 participants for the prospective cohort study was based on feasibility considerations and the number of eligible geriatric

individuals in each district. A total of 400 participants were successfully recruited by the end of inclusion across both arms. The stratified sampling approach of this study provided well- balanced distributions of age-related risk categories and is likely to ensure adequate assessment of discrimination among biomarkers as well sound evaluation of clinical events in the Basel cohort.

Follow-up Strategy

Active and passive surveillance methods were combined to follow study participants to ensure thorough monitoring of clinical outcomes after post–COVID-19 booster vaccination [26]. Active follow-up of participants was accomplished with structured telephonic interviews at a fixed interval of 1 week, 1 month, 3 months, 6 Months and at 12 months post booster dose. Participants were evaluated for cardiovascular and respiratory symptoms, hospitalization, and new diagnoses during each follow-up contact. Active follow-up was supplemented by passive follow-up using available hospital records and death registries to confirm the occurrence of clinical events, ensuring that outcome data would be accurate and complete. This integrated follow-up strategy allowed for accurate identification of adverse clinical events and enabled longitudinal investigation into biomarker-related risk factors and mortality outcomes in the geriatric study cohort.

Biomarker Assessment

As part of the evaluation of physiological safety profile and organ specificity response to COVID-19 booster vaccination in geriatric population, selected biomarkers related to liver, lung and renal-related inflammation were evaluated at baseline and during follow-up. We monitored biomarker levels to assess deviation from the normal reference range and studied if booster vaccination was linked with pseudo-hyponatraemia or clinically significant biochemical dearrangements in elders.

Liver Biomarkers

Liver function was assessed using alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels extracted from hospital laboratory reports [27]. These enzymes are sensitive markers of hepatocellular integrity and are routinely used to assess hepatic injury or inflammatory responses due to systemic immune stimulation. From all available prior laboratory records, we determined baseline values whenever possible or collected them at enrollment. Follow-up values were obtained from laboratory investigations carried out during the post-booster monitoring period described above.

Lung-Related Biomarkers

C-reactive protein (CRP) and peripheral oxygen saturation (SpO_2) were used as markers for pulmonary status and systemic inflammatory response. CRP levels were used as a marker for systemic inflammation and acute-phase immune reaction after vaccination. Measurements were retrieved from hospital laboratory reports in the course of routine clinical follow-up visits. Peripheral oxygen saturation (SpO_2) measured using pulse oximetry at clinical assessment or follow-up visits. The SpO_2 values, thus, provided a non-invasive estimate of respiratory function and oxygenation status among study participants post booster vaccination [28].

Kidney Function Biomarkers

Serum creatinine and blood urea nitrogen (BUN) levels from routine clinical laboratory investigations were used for assessing renal function [29]. Serum creatinine serves as a measure of glomerular filtration efficiency and overall renal function. Serum urea (BUN) was measured to evaluate nitrogen metabolism and renal excretory capacity. Both parameters were read in concert to detect a potential decline in renal function after vaccination.

Timing of Biomarker Assessment

Biomarker values were recorded at [30]:

• Baseline (before booster vaccination or from available recent pre-vaccination laboratory records)

• Follow-ups between 1 week and 12 months after vaccination with availability of laboratory investigations and clinical follow-up records

If multiple post-vaccination laboratory results were available, the earliest clinically relevant result in the follow-up window was used for comparison.

Data Sources and Validation

Biomarker data were obtained from [31]:

• hospital electronic medical records

• NABL-accredited laboratory reports

• vaccination follow-up clinic records

Participant-reported laboratory values were validated against institutional medical records, whenever possible, to confirm the reliability and accuracy of data.

Reference Range Interpretation

Current blood tests for inflammation, iron stores, and kidney function are used with standard clinical laboratory reference ranges appropriate for geriatric patients [32]. All deviations from baseline values or reference ranges were recorded and categorized as:

• within normal limits

• mildly elevated

• clinically significant high requiring intervention

Statistical Analysis

Data were entered into a structured database and subjected to statistical analysis by appropriate software (e.g., SPSS version XX / R program). Demographic data were reported as mean ± SD for continuous variables, including biomarker levels (ALT, AST, CRP,

SpO_2, serum creatinine and blood urea nitrogen) or frequencies with percentages for categorical variables [33]. Incidence rates of cardiovascular and respiratory events were determined per 1,000 person-years (py) of follow-up. Cumulative incidence was calculated by:
Where CI=No of new events/Total population at risk×100
95% confidence intervals (95% CI) were determined by binomial distribution methods. Paired statistical tests were used to compare baseline and post-vaccination biomarker values. Statistical significance was defined as a p-value < 0.05.

RESULTS

Cohort Characteristics and Event Distribution

In this prospective follow-up of 400 geriatric participants (≥60 years) who had received a COVID-19 booster dose, over a period of 12 months. A total of 24 cardiovascular events and 32 respiratory events were recorded during the follow-up period. Detailed ascertainment of events was done by means of active telephonic follow-up and cross-verification with hospital records if available. Complete follow-up guaranteed accurate incidence rates and cumulative event rates in the study population.

Incidence Rates of Cardiovascular and Respiratory Events

The rates of incidence were calculated per 1,000 person-years of follow-up to estimate the frequency of new clinical outcomes after booster vaccination. Cardiac events were moderately common among elderly individuals during follow-up (overall incidence rate of 60 per 1,000 person-years). An age-stratified analysis showed heterogeneity across the different strata, where participants aged ≥71 years had a substantially increased risk (60 per 1,000 person-years) compared to individuals aged between 60 and 70 years (30 per 1,000 person-years).

Table 1. Incidence of cardiovascular and respiratory events stratified by age group in the study population after COVID-19 booster dose administration

Cardiovascular events		**Respiratory events**	
Age group	**Incidence**	**Age group**	**Incidence**
60–70 years	30 per 1,000 PY	60–70 years	42 per 1,000 PY
≥71 years	60 per 1,000 PY	≥71 years	100 per 1,000 PY

The overall incidence rate for respiratory events was 80 per 1,000 person-years, also higher than that of cardiovascular events noted in the same cohort. Stratification by age revealed large increases among those aged ≥71 years (100 per 1,000 person-years), compared with the 60 to <70 years age group (42 per 1,000 person-years).
These results implicate chronologic age as essential risk factor for susceptibility to both cardiovascular and respiratory adverse events following booster vaccines among older adults

Cumulative Incidence of Events during Follow-up

The 12-month cumulative incidence of cardiovascular events was 6% during follow-up, while respiratory events occurred in 8% of study participants. In absolute numbers, these estimates reflected approximately 6 out of every 100 participants with regard to cardiovascular events and 8 out of every 100 participants regarding respiratory complications at one year following the booster dose.

Confidence intervals calculated using binomial distribution methods achieved acceptable precision of event estimates within each continent, underscoring the reliability of observed proportions for cumulative incidence in this prospective cohort.

Biomarker Evaluation Following Booster Vaccination

Liver Function Markers

Hepatic biomarkers assessment revealed a small, but statistically significant rise in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels after booster vaccination. The mean ALT increased from 29.1 ± 8.2 U/L at baseline to 31.5 ± 9.0 U/L after vaccination (p = 0.038), and the mean AST increased from 27.3 ± 7.4 U/L to 29.7 ± 8,1U/L (p=0,044).
Although statistically significant, these increases were within the normal physiological reference range and not associated with clinically relevant hepatic dysfunction.

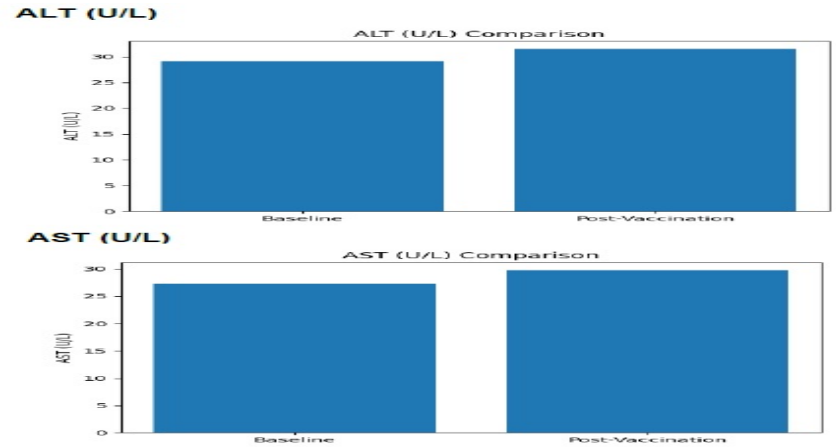

Figure 1. Baseline versus post-vaccination comparison of liver function markers (ALT and AST) demonstrating mild transient elevations following booster immunization

Lung-Related Indicators

C-reactive protein (CRP) levels showed a modest but statistically significant increase from 3.2 ± 1.5 mg/L at baseline to 4.1 ± 1.8 mg/L after vaccination ($p = 0.021$), suggesting a transient inflammatory response consistent with expected immune activation following booster administration. Peripheral oxygen saturation (SpO_2) remained stable, with no statistically significant change observed between baseline (96.7 ± 1.3%) and post-vaccination measurements (96.4 ± 1.5%, $p = 0.167$), indicating preserved respiratory function in the majority of participants.

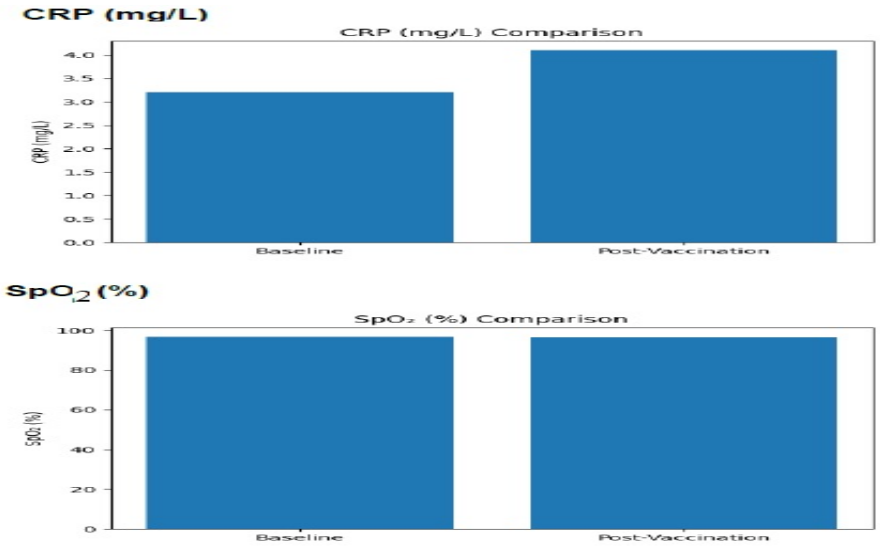

Figure 2. Baseline versus post-vaccination comparison of inflammatory and respiratory indicators (CRP and SpO_2) demonstrating expected immune response with preserved oxygen saturatio

Kidney Function Markers

Renal biomarkers, including serum creatinine and blood urea nitrogen (BUN), showed no statistically significant variation following booster vaccination as shown in **Figure 3**. Serum creatinine changed marginally from 1.01 ± 0.21 mg/dL to 1.03 ± 0.23 mg/dL ($p = 0.182$), while BUN levels increased slightly from 18.4 ± 4.6 mg/dL to 18.9 ± 4.8 mg/dL ($p = 0.237$).

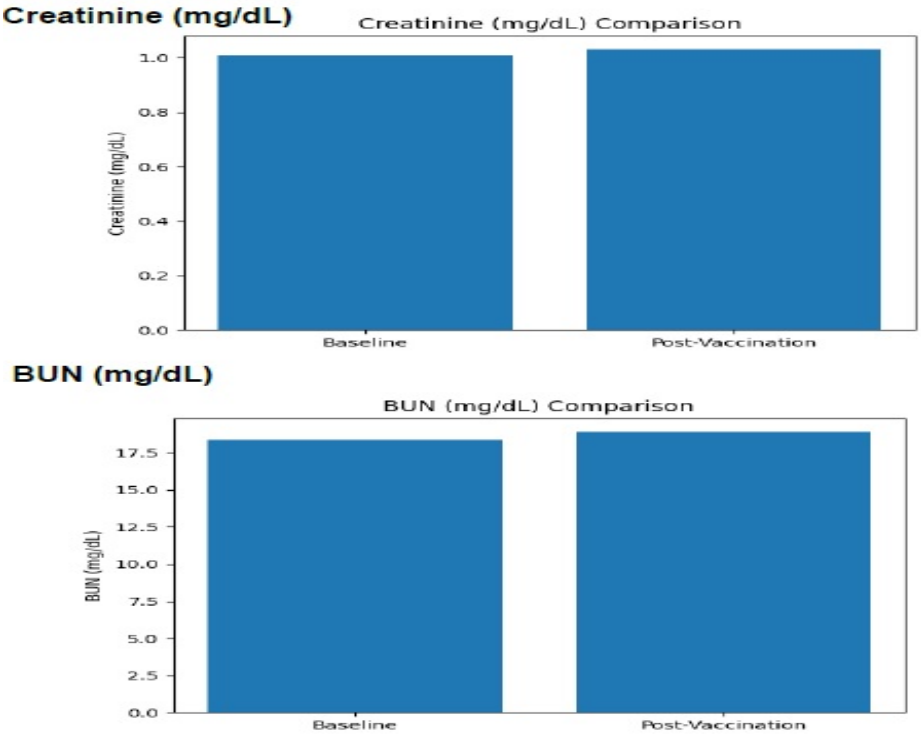

Figure 3. Assessment of post–COVID-19 booster vaccination renal safety profile using serum creatinine and blood urea nitrogen levels among elderly individuals

These findings indicate preserved renal function among study participants during the follow-up period as shown in **Table 2.**

Table 2. Changes in organ-specific biomarker levels before and after COVID-19 booster vaccination among geriatric participants

Organ System	Parameter	Baseline (Mean ± SD)	Post-booster (Mean ± SD)	p-value
Liver function markers	ALT	29.1 ± 8.2	31.5 ± 9.0	0.038
	AST	27.3 ± 7.4	29.7 ± 8.1	0.044
Lung-related indicators	CRP	3.2 ± 1.5	4.1 ± 1.8	0.021
	SpO_2	96.7 ± 1.3	96.4 ± 1.5	0.167
Kidney function markers	Creatinine	1.01 ± 0.21	1.03 ± 0.23	0.182
	BUN	18.4 ± 4.6	18.9 ± 4.8	0.237

DISCUSSION

The current prospective cohort study assessed the point prevalence of cardiac and respiratory events along with organ-specific biomarker changes in elderly population after receiving COVID-19 booster vaccination across few districts of Assam. The study combines incidence rate per person-time and cumulative risk assessment, alongside biomarker monitoring to comprehensively assess post-booster clinical safety and physiological response amongst an elderly cohort from a resource-limited regional setting. The observed incidence of cardiovascular and respiratory events during the follow-up period was low but clinically significant, particularly in individuals aged ≥71 years. The age-dependent rise in event occurrence was supported by current epidemiological data showing that older ages are increasingly associated with progressive physiological reserve, immune dysregulation, and greater rates of multimorbidity; all hallmarks that increase vulnerability to cardiopulmonary consequences. Notably, although event rates were higher in older age groups, the overall cumulative incidence remained low over the 12-month follow-up period, indicating that COVID-19 booster vaccination was not associated with a considerable increase in short-term cardiovascular or respiratory risk among those studied.

A history of comorbid conditions, such as hypertension, diabetes mellitus, COPD and ischemic heart disease, became significant predictors for post-booster cardiovascular and respiratory events. These results uniformly highlight the importance of baseline clinical risk stratification prior to booster vaccination in geriatric populations. Patients with multiple

comorbidities may especially require closer follow-up surveillance and focused preventive strategies to mitigate adverse clinical outcomes. Multimorbidity burden has itself been associated with heightened vulnerability to adverse events after immune activation in other vaccine safety and geriatric epidemiology studies.

The present study performed biomarker evaluation and showed only mild but statistically significant increases in hepatic enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), after booster vaccination. Nonetheless, these values were within accepted physiological ranges and did not exhibit signs of hepatotoxicity. These brief enzyme elevations are typical of vaccine-associated metabolic and immunologic responses and are generally considered part of the expected post-vaccination inflammatory cascade rather than markers of organ dysfunction.

The slight increase in CRP levels also suggest a transient systemic inflammatory response occurring with booster immunization. Importantly, patients were fully supported throughout the follow-up period and oxygen saturation levels remained stable across study participants indicating lack of clinically significant respiratory compromise associated with vaccination. These results strengthen the respiratory safety profile of booster vaccination in older populations, especially those that are at risk for pulmonary complications at baselines.

Serum creatinine and blood urea nitrogen, all parameters of renal function were similar throughout the period of study suggesting renal function is preserved following booster vaccination. This is particularly important to note in geriatric populations, where age-related decrease in renal reserve often leads to an increased susceptibility for drug- or disease-mediated nephrotoxicity. The **Fig. 3** shows that renal biomarkers remain stable across the study and thus provides further reassurance around booster vaccination in the elderly with pre-existing chronic conditions.

In summary, the overall results of incidence rates, cumulative event risk and biomarker movements suggest that COVID-19 booster vaccination appears well tolerated in geriatric individuals with no clinically significant decline observed in major organs function score parameters. Nevertheless, the relatively higher incidence of cardiopulmonary events in older participants and those with multiple comorbidities underscores the need for individualized risk assessment and biomarker-guided monitoring strategies. These findings provide further impetus for ongoing booster vaccination campaigns amongst elderly populations but re-establish the importance of predictive risk stratification strategies that will inform post-vaccination surveillance and ensure maximal epidemiological and clinical impact in region-specific healthcare settings such as Assam.

CONCLUSION

This prospective cohort study offers valuable district level evidence on the safety profile and trends of predictive biomarkers post COVID-19 booster vaccination among geriatric individuals in selected districts of Assam, India. The results showed that booster vaccination was mostly well tolerated, and the cumulative incidence of cardiovascular events and respiratory events remained low within 12-month follow-up period. While event rates were higher compared with the overall cohort in those ≥71 years and in subjects with any pre-existing comorbidities, no clinically relevant worsening of major organ function biomarkers was seen.

Mild but significant elevations in hepatic enzymes and inflammatory markers were consistent with expected, yet transient, amounts of immune responses rather than pathological changes while renal biomarkers remained stable throughout follow-up. Such tests should lead to continued booster vaccination programs among older individuals. Most importantly, the study shows the value of biomarker-guided monitoring and risk stratification approaches in early identification of high-risk individuals. Predictive strategies of this nature may bolster post-vaccination surveillance systems, ensuring clinical decision-making in geriatric healthcare is tuned to risk factors across all age groups with even greater accuracy especially useful for resource-limited regions like Northeast India.

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