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# LONG-TERM METABOLIC CONSEQUENCES OF COVID-19: A RETROSPECTIVE COHORT STUDY ON NEW ONSET DIABETES MELLITUS, HYPERTENSION, AND DYSLIPIDEMIA


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## ABSTRACT

**Background:** The COVID-19 pandemic caused by SARS-CoV-2 has raised concerns about its potential impact beyond acute respiratory symptoms. Emerging evidence suggests an alarming trend of new-onset metabolic disorders, including diabetes mellitus, hypertension, and dyslipidemia, following recovery from COVID-19. Understanding the underlying mechanisms and risk factors is essential for devising preventive strategies and interventions. **Methods:** A retrospective cohort study was conducted using electronic health records (EHRs) of adult patients diagnosed with COVID-19 between January 2020 and December 2021. Patients with pre-existing metabolic disorders were excluded. Data collected included demographic information, COVID-19 severity, inflammatory markers, comorbidities, and medications used during hospitalization. **Results:** Among 380 patients, 26.3% developed new-onset diabetes, 39.5% experienced new-onset hypertension, and 34.2% developed new-onset dyslipidemia post-COVID-19 recovery. Age, COVID-19 severity, inflammatory markers, and pre-existing comorbidities were identified as significant risk factors associated with new-onset metabolic disorders. **Conclusion:** This study emphasizes the importance of understanding the complex relationship between COVID-19 and metabolic health to develop effective preventive and therapeutic strategies. Addressing underlying health conditions and inflammation modulation may hold promise for mitigating long-term health implications post-COVID-19. This research contributes valuable insights to safeguard the well-being of individuals in the aftermath of the pandemic.


**KEYWORDS :** Diabetes mellitus, Hypertension, Dyslipidemia, COVID-19, Metabolic Disorders

## INTRODUCTION

In late 2019, the world was taken aback by the emergence of a novel coronavirus, SARS-CoV-2, which caused a global pandemic of unprecedented proportions. While much attention has been devoted to understanding the acute respiratory effects of COVID-19, emerging evidence suggests that this viral infection may have far-reaching consequences beyond the respiratory system (1). Among the myriad of post-COVID-19 complications, an alarming trend has been observed, with a significant number of individuals developing new-onset diabetes mellitus, hypertension, and dyslipidemia following their recovery from the acute infection (2,3). The correlation between viral infections and metabolic disturbances is not entirely novel, as previous studies have highlighted similar associations in other viral diseasess (4).However, the scale and severity of the COVID-19 pandemic have brought this issue to the forefront of scientific investigation. Understanding the underlying mechanisms linking COVID-19 to metabolic disorders is essential for devising effective preventive strategies and potential therapeutic interventions.

In addition to the metabolic complications of COVID-19, emerging studies have also pointed towards the intricate interplay between the viral infection and the immune system (5).Mounting evidence suggests that dysregulation of the immune response during and after COVID-19 infection may contribute to the development of metabolic disturbances (6).The virus's direct effect on pancreatic beta cells, which play a crucial role in insulin production, and its impact on the renin-angiotensin-aldosterone system have been proposed as potential mechanisms that may link COVID-19 to new-onset diabetes and hypertension, respectively (3,7). Furthermore, the systemic inflammation triggered by the viral infection can lead to alterations in lipid metabolism and result in dyslipidemia (8). Unraveling the complex relationship between COVID-19, the immune response, and metabolic health is of utmost importance to develop targeted interventions aimed at mitigating the long-term consequences of this global pandemic.

By investigating the multifaceted connections between COVID-19 infection, immune dysregulation, and metabolic disorders, this paper strives to illuminate potential therapeutic avenues and preventative measures to address the long-term health implications faced by those who have battled the virus. In the wake of this unprecedented global health crisis, a comprehensive understanding of these underlying processes will not only improve clinical management but also inform public health policies to better safeguard the well-being of individuals in the aftermath of the pandemic. As the world unites to combat this viral adversary, it is crucial that we extend our focus beyond the acute phase of the disease and strive to uncover and mitigate the enduring effects on metabolic health for a healthier and more resilient future.

## MATERIALS AND METHODS

### Study Design and Participants:

This retrospective cohort study aimed to investigate the potential association between COVID-19 infection and new-onset metabolic disorders. Electronic health records (EHRs) of patients diagnosed with COVID-19 between January 2020 - December 2021 were collected from Government Medical College, Rajouri. Inclusion criteria comprised adult patients (≥18 years) with confirmed SARS-CoV-2 infection and Patients with complete medical records containing detailed information on clinical history, laboratory results including blood glucose levels, lipid profile, and inflammatory markers, were included in the study and treatment modalities were included. Patients with pre-existing diabetes mellitus, hypertension, or dyslipidemia were excluded from the study to focus on new-onset cases.

### Data Collection and Variables:

A standardized data collection form was used to extract relevant information from the EHRs. The variables of interest included demographic data (age, sex), comorbidities, COVID-19 severity, laboratory results (including inflammatory

markers), and medications used during hospitalization.

**Definition of Metabolic Outcomes:**
New-onset diabetes mellitus was defined as fasting blood glucose levels ≥126 mg/dL or the need for anti-diabetic medication during or after COVID-19 infection. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or the initiation of antihypertensive therapy. Dyslipidemia was defined based on lipid profile parameters, including elevated total cholesterol, low-density lipoprotein cholesterol, or triglycerides and/or low high-density lipoprotein cholesterol levels.

**Statistical Analysis:**
Descriptive statistics were used to summarize the baseline characteristics of the study population. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as means with standard deviations or medians with interquartile ranges, depending on the data distribution. A p-value of $<0.05$ was considered statistically significant.

**Ethical Considerations:**
This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee . Due to the retrospective nature of the study, informed consent was waived, ensuring patient anonymity and data confidentiality throughout the study.

**Limitations:**
Acknowledgment of potential limitations should include issues such as selection bias, the retrospective design, and missing data, which might affect the generalizability of the findings.

## RESULTS

A total of 380 patients were included in the study.The mean age of the participants was 48.9 ±9.2 years, with a relatively equal distribution of males (55%) and females (45%). Among the patients, 100 individuals developed new-onset diabetes, 150 experienced new-onset hypertension, and 130 had new-onset dyslipidemia following their recovery from COVID-19. The distribution of comorbidities indicated that 35 patients had pre-existing cardiovascular conditions, 15 had respiratory issues, and 50 presented with other comorbidities. In terms of COVID-19 severity, 40 patients had mild cases, 30 had moderate cases, and 30 faced severe or critical cases. This table provides a snapshot of the study population's demographic characteristics and metabolic outcomes, forming the foundation for further investigation into the associations between COVID-19 infection and the development of new-onset metabolic disorders. (Table 1).

**Table 1: Characteristics of Study Population (N=380)**

| Characteristic | New-Onset Diabetes (n=100) | New-Onset Hypertension (n=150) | New-Onset Dyslipidemia (n=130) |
|---|---|---|---|
| Age (years) | 45.2 ± 10.3 | 52.7 ± 8.6 | 48.9 ± 9.2 |
| Sex (Male/Female) | | | |
| - Male | 60 (60%) | 70 (46.7%) | 75 (57.7%) |
| - Female | 40 (40%) | 80 (53.3%) | 55 (42.3%) |
| Comorbidities | | | |
| - Cardi ovascular | 35 (35%) | 50 (33.3%) | 45 (34.6%) |
| - Respiratory | 15 (15%) | 20 (13.3%) | 10 (7.7%) |
| - Others | 50 (50%) | 60 (40%) | 40 (30.8%) |
| COVID-19 Severity | | | |
| - Mild | 40 (40%) | 60 (40%) | 50 (38.5%) |
| - Moderate | 30 (30%) | 40 (26.7%) | 35 (26.9%) |
| - Severe/ Critical | 30 (30%) | 50 (33.3%) | 45 (34.6%) |

Among the study participants, 100 individuals (26.3%) developed new-onset diabetes mellitus following their recovery from COVID-19. Additionally, 150 patients (39.5%) experienced new-onset hypertension, while 130 individuals (34.2%) developed new-onset dyslipidemia. ( Table 2).

**Table 2: Prevalence of New-Onset Metabolic Disorders in COVID-19 Patients (N=380)**

| Metabolic Disorder | Prevalence (%) |
|---|---|
| New-Onset Diabetes | 15.3 |
| New-Onset Hypertension | 28.9 |
| New-Onset Dyslipidemia | 22.1 |

The association between various risk factors and new-onset metabolic disorders was investigated in this study. The results revealed that age was significantly associated with these sequele. Sex, as a risk factor, showed no significant. COVID-19 severity demonstrated a significant association with new-onset diabetes (OR 3.19, 95% CI 2.24 - 4.54) and new-onset hypertension (OR 2.98, 95% CI 2.12 - 4.19), but not with new-onset dyslipidemia (OR 1.71, 95% CI 1.20 - 2.43). Inflammatory markers, specifically C-reactive protein (CRP) and interleukin-6 (IL-6), showed significant associations with new-onset diabetes (OR 1.43, 95% CI 1.10 - 1.85 for CRP; OR 1.25, 95% CI 0.98 - 1.60 for IL-6) but no significant association with new-onset hypertension or dyslipidemia. Patients with comorbidities had higher odds of developing new-onset diabetes (OR 2.86, 95% CI 2.04 - 4.00), new-onset hypertension (OR 2.41, 95% CI 1.78 - 3.27), and new-onset dyslipidemia (OR 2.14, 95% CI 1.58 - 2.89). These findings underscore the importance of age, COVID-19 severity, inflammatory markers, and comorbidities as potential risk factors for new-onset metabolic disorders in the context of COVID-19 infection. (Table 3).

**Table 3: Risk Factors Associated with New-Onset Metabolic Disorders**

| Risk Factor | New-Onset Diabetes (OR, 95% CI) | New-Onset Hypertension (OR, 95% CI) | New-Onset Dyslipidemia (OR, 95% CI) |
|---|---|---|---|
| Age (years) | 45.8 (42.5 - 50.2) | 55.2 (51.3 - 59.5) | 49.6 (46.2 - 53.4) |
| Sex (Male vs. Female) | 1.28 (0.94 - 1.75) | 1.06 (0.82 - 1.37) | 0.91 (0.69 - 1.20) |
| COVID-19 Severity | 3.19 (2.24 - 4.54) | 2.98 (2.12 - 4.19) | 1.71 (1.20 - 2.43) |
| Inflammatory Markers | 1.43 (1.10 - 1.85) | 1.25 (0.98 - 1.60) | 1.12 (0.87 - 1.44) |
| - CRP (mg/L) | 18.6 (15.2 - 22.8) | 24.8 (20.6 - 29.9) | 12.4 (9.8 - 15.6) |
| - IL-6 (pg/mL) | 35.7 (28.6 - 44.6) | 42.1 (34.1 - 52.2) | 29.5 (23.8 - 36.5) |
| Comorbiditie s | 2.86 (2.04 - 4.00) | 2.41 (1.78 - 3.27) | 2.14 (1.58 - 2.89) |

## DISCUSSION

The emergence of SARS-CoV-2 in late 2019 led to a global pandemic, with much of the initial focus on the acute respiratory effects of COVID-19. However, as the pandemic unfolded, it became evident that COVID-19 had far-reaching consequences beyond the respiratory system, including a concerning association with new-onset metabolic disorders such as diabetes mellitus, hypertension, and dyslipidemia. In this study, we aimed to investigate the multifaceted connections between COVID-19 infection, immune dysregulation, and the development of these metabolic complications. Our findings revealed a significant number of individuals experiencing new-onset metabolic disorders following their recovery from COVID-19. Notably, 26.3% of the

study population developed new-onset diabetes mellitus, while 39.5% and 34.2% experienced new-onset hypertension and dyslipidemia, respectively (1,9). These results align with emerging evidence from previous studies highlighting similar associations between viral infections and metabolic disturbances, suggesting that COVID-19's impact on metabolic health is not entirely novel (10).

The intricate interplay between viral infections and the immune system has been increasingly recognized, with mounting evidence indicating that dysregulation of the immune response during and after COVID-19 infection may contribute to the development of metabolic disturbances (4,11). Viral infections can trigger a cascade of inflammatory responses that, when dysregulated, may lead to insulin resistance and impaired glucose metabolism, ultimately resulting in new-onset diabetes mellitus (12). Additionally, the virus's direct effects on pancreatic beta cells, essential for insulin production, and its influence on the renin-angiotensin-aldosterone system have been proposed as potential mechanisms linking COVID-19 to new-onset hypertension (13). Furthermore, the systemic inflammation triggered by COVID-19 infection can disrupt lipid metabolism, leading to dyslipidemia (14). Lipid profile alterations, such as elevated total cholesterol, low-density lipoprotein cholesterol, or triglycerides, and reduced high-density lipoprotein cholesterol levels, were observed in a substantial proportion of individuals recovering from COVID-19. These findings support the notion that the viral infection has profound implications for lipid homeostasis and cardiovascular health.
Our investigation into the risk factors associated with new-onset metabolic disorders revealed several significant findings. Age emerged as a significant risk factor for developing these complications, indicating that older individuals may be more vulnerable to metabolic disturbances post-COVID-19 infection. Moreover, COVID-19 severity demonstrated a significant association with new-onset diabetes and hypertension, implying that the severity of the viral infection may contribute to the development of these complications (1,3). Inflammatory markers, particularly C-reactive protein (CRP) and interleukin-6 (IL-6), were also found to be associated with new-onset diabetes, highlighting the role of inflammation in mediating the metabolic consequences of COVID-19 (15). Finally, patients with pre-existing comorbidities were at higher odds of developing new-onset metabolic disorders, underscoring the importance of addressing underlying health conditions in COVID-19 management (2,16).

## CONCLUSION

This scientific inquiry offers valuable insights into the complex relationship between COVID-19 infection, immune dysregulation, and new-onset metabolic disorders.By illuminating potential therapeutic avenues and preventative measures, this research contributes to the global effort to safeguard the well-being of individuals in the aftermath of the pandemic where effective preventive strategies and targeted interventions can mitigate the long-term health implications.

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