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A RETROSPECTIVE COMPARATIVE ANALYSIS OF THE TEMPORAL DYNAMICS OF ACUTE CORONARY SYNDROMES DURING THE PERI-PANDEMIC (COVID-19) PERIOD

PERİ-PANDEMİ (COVID-19) DÖNEMİNDE AKUT KORONER SENDROMLARIN ZAMANSAL DİNAMİKLERİNİN RETROSPEKTİF KARŞILAŞTIRMALI ANALİZİ

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ABSTRACT

Objective: The COVID-19 pandemic, caused by SARS-CoV-2, disrupted global healthcare systems and significantly influenced cardiovascular health. This study examines the temporal trends of acute coronary syndromes (ACS), including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris (USAP), across pre-pandemic, pandemic, and post-pandemic periods.

Methods: This retrospective observational study was conducted at a single tertiary cardiovascular center involving patients diagnosed with ACS from January 2018 to June 2024. Patients were stratified into three cohorts: pre-pandemic (January 2018-February 2020), pandemic (March 2020-April 2022), and post-pandemic (May 2022-June 2024).

Results: The incidence of STEMI and NSTEMI significantly increased in the post-pandemic period compared to those in the other periods ($p<0.001$). The number of USAP cases was significantly lower during the pandemic and post-pandemic periods ($p<0.01$). Temporal analyses revealed a positive correlation between time and STEMI/NSTEMI cases ($p<0.0001$). However, USAP incidence showed no significant correlation with time. These trends suggest that delayed healthcare access and pandemic-related inflammatory and thrombotic mechanisms are key drivers of increased myocardial infarction cases.

Conclusion: The findings underscore the enduring impact of the pandemic on ACS presentations, highlighting the need for adaptive healthcare systems. Strategies incorporating anti-inflammatory approaches and resilient healthcare frameworks are essential for mitigating the long-term cardiovascular consequences of future crises. Further multicenter studies are recommended to validate these findings and to enhance our understanding of the mechanisms involved.

Keywords: Acute coronary syndromes, COVID-19, NSTEMI, STEMI, USAP

ÖZ

Amaç: SARS-CoV-2'nin neden olduğu COVID-19 pandemisi, küresel sağlık sistemlerini ciddi şekilde etkileyerek kardiyovasküler sağlığı derinden etkilemiştir. Bu çalışma, pandemi öncesi, pandemi ve pandemi sonrası dönemlerde ST-yükselmeli miyokard enfarktüsü (STEMI), ST-yükselmesiz miyokard enfarktüsü (NSTEMI) ve stabil olmayan angina pektoris (USAP) gibi akut koroner sendromların (AKS) zamansal eğilimlerini değerlendirmektedir.

Yöntem: Bu retrospektif gözlemsel çalışma, Ocak 2018 ile Haziran 2024 tarihleri arasında bir üçüncü basamak kardiyovasküler merkezde AKS tanısı alan hastaları içermektedir. Hastalar üç kohorta ayrılmıştır: pandemi öncesi (Ocak 2018-Şubat 2020), pandemi (Mart 2020-Nisan 2022) ve pandemi sonrası (Mayıs 2022-Haziran 2024).

Bulgular: STEMI ve NSTEMI insidansı, diğer dönemlere kıyasla pandemi sonrası dönemde anlamlı şekilde artmıştır ($p<0,001$). USAP vakalarının sayısı ise pandemi ve pandemi sonrası dönemlerde anlamlı olarak daha düşüktür ($p<0,01$). Zamansal analiz, STEMI/NSTEMI vakaları ile zaman arasında pozitif bir korelasyon olduğunu göstermiştir ($p<0,0001$). Ancak USAP insidansı ile zaman arasında anlamlı bir korelasyon saptanmamıştır. Bu eğilimler, pandemiye bağlı gecikmiş sağlık hizmetlerine erişim ile inflamatuvar ve trombotik mekanizmaların miyokard enfarktüsü vakalarındaki artışın ana nedenleri olduğunu ortaya koymaktadır.

Sonuç: Bulgular, pandeminin AKS sunumları üzerindeki kalıcı etkisini vurgulamakta ve adaptif sağlık sistemlerine duyulan ihtiyacı işaret etmektedir. Gelecekteki krizlerin uzun vadeli kardiyovasküler sonuçlarını azaltmak için anti-inflamatuvar yaklaşımlar içeren stratejiler ve dirençli sağlık sistemleri gereklidir. Bu bulguların doğrulanması ve ilgili mekanizmaların daha iyi anlaşılması için çok merkezli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Akut koroner sendromlar, COVID-19, NSTEMI, STEMI, USAP

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Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has profoundly affected global healthcare systems, extending far beyond its well-characterized respiratory pathology to impose significant burdens on cardiovascular health.[1] COVID-19 is progressively recognized as a multi-systemic disease with significant complications for the cardiovascular system, including heightened risks of myocardial infarction (MI), thrombotic events, and other major adverse cardiac events (MACE).[2] The pathophysiology of myocardial injury in the context of COVID-19 is multifaceted, encompassing both direct and indirect mechanisms. These include viral infiltration of cardiomyocytes, exacerbated systemic inflammatory responses, endothelial dysfunction, and the induction of a hypercoagulable state.[3] Collectively, these interrelated mechanisms have exacerbated the global burden of cardiovascular disease during the pandemic. Both the acute and chronic sequelae of COVID-19 on cardiovascular health are marked by an increased incidence of acute coronary syndromes (ACS), including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris (USAP).[4-6]

Acute MI, defined as sustained myocardial ischemia culminating in irreversible myocardial necrosis, persists as a principal contributor to global morbidity and mortality.[7] The COVID-19 pandemic has further illuminated the complex interrelationship between systemic inflammatory cascades and underlying cardiovascular comorbidities, underscoring an augmented incidence and severity of MI presentations.[1,8] Direct viral infiltration into endothelial cells precipitates widespread endothelitis, which, in turn, contributes to atherosclerotic plaque instability and thrombotic complications.[9] In addition, the systemic hyperinflammatory response, characterized by the so-called cytokine storm, coupled with a hypercoagulable state, predisposes patients to ACS.[10,11] Pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), play critical roles in endothelial dysfunction, fostering plaque rupture and subsequent myocardial injury.[12-14]

In addition to the direct pathophysiological consequences of SARS-CoV-2 infection, the indirect effects of the pandemic have profoundly impacted cardiovascular outcomes.[15,16] Delays in seeking emergency medical care, driven by the fear of contacting SARS-CoV-2, along with extensive disruptions in healthcare delivery, has resulted in delays in seeking emergency medical care for acute cardiovascular events. Such delays have contributed to increased rates of out-of-hospital cardiac arrest and worsened clinical presentations upon hospital admission.[17] Additionally, decreased access to healthcare services, compounded by an overwhelming burden on healthcare infrastructure, has led to suboptimal management of ACS during the pandemic, resulting in increased in-hospital mortality and adverse clinical outcomes.[18]

The incidence of ACS, including STEMI, NSTEMI, and USAP, has demonstrated significant temporal variability throughout the various phases of the pandemic. Retrospective analyses have documented a notable decline in hospital admissions for ACS during the initial stages of the pandemic, followed by a subsequent increase in the incidence of delayed presentations and associated complications.[19-21] Nevertheless, a comprehensive evaluation of ACS incidence spanning the pre-pandemic, pandemic, and post-pandemic periods remains limited. This gap constrains our ability to fully understand of how healthcare disruptions and viral pathogenicity collectively influence cardiovascular health. The present study aims to undertake a rigorous retrospective evaluation of the incidence of acute coronary syndromes during the COVID-19 pandemic, with comparative analyses involving the pre-pandemic and post-pandemic periods.

Methods

This retrospective observational study was conducted at a single tertiary cardiovascular center, involving patients diagnosed with ACS from January 2018 to June 2024. All adult patients who were diagnosed with ACS based on clinical symptoms and signs, electrocardiography (ECG) changes, cardiac biomarker evaluation and who underwent coronary angiography were included in the study.

In the present study, STEMI was defined as the detection of ST-segment elevation (or ST-segment elevation equivalent) on the ECG of a patient with ischemic symptoms. NSTEMI was defined as the detection of elevated cardiac injury markers without ST-segment elevation on the ECG of a patient with ischemic symptoms. USAP was defined as myocardial ischemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis. Angina lasting more than 20 minutes at rest, new-onset severe angina, and angina with increasing frequency and duration were also considered USAP. Patients with incomplete clinical records, those who did not undergo coronary angiography, and those who experienced in-hospital mortality unrelated to cardiovascular causes were excluded.

The first COVID-19 case was reported on March 11, 2020 by the Ministry of Health of the Republic of Türkiye. When the two-week incubation period of the virus is also taken into account, according to official statements, the period before March 2020 in Türkiye was considered as the pre-pandemic period; the period when protective measures, including masks, were increased and a full lockdown was experienced was considered as the pandemic period; and the period after April 2022, when strict measures were relaxed and many obligations due to the pandemic were officially lifted, was considered as the post-pandemic period. Accordingly, the patients

were categorized into three temporal cohorts based on their admission period: pre-pandemic (January 2018 to February 2020), pandemic (March 2020 to April 2022), and post-pandemic (May 2022 to June 2024). The study was approved by the Amasya University Non-Interventional Clinical Research Ethics Committee (Date: 26 November 2024, No: 2024/123).

Data Collection and Measured Outcomes

Patient data were retrospectively collected from the electronic health records (EHRs) of the hospital. Temporal cohort assignment was based on the date of hospital admission. The outcome was the incidence of ACS during the pre-pandemic, pandemic, and post-pandemic periods. All included subjects had valid and complete information for all study variables. Our hospital is the only hospital in the city, and the cardiology department accepts patients and performs coronary angiography procedures on a 7/24 basis. Before, during and after the pandemic, a limited number of patient referrals were made to other centers with higher bed capacity nearby, but the number of referrals did not differ in the relevant periods.

Statistical Analysis

The statistical analyses were conducted using SPSS software (version 27.0; SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation. The Kolmogorov-Smirnov test was used to evaluate the normality of the data distribution. One-way analysis of variance (ANOVA) was performed for intergroup comparisons of variables with a normal distribution, followed by Tukey's post-hoc test for multiple comparisons. Data that did not follow a normal distribution were analyzed using the Kruskal-Wallis test, followed by Dunn's multiple comparison test. Correlation analyses were performed using Pearson's correlation test for parametric data, and Spearman's correlation test for nonparametric data. A p value of <0.05 was considered indicative of statistical significance.

Results

The total number of ACS cases during the pre-pandemic, pandemic and post-pandemic periods were 1860, 1488 and 2216, respectively. A total of 431, 456 and 617 patients were diagnosed with STEMI, 954, 872 and 1303 were diagnosed with NSTEMI, and 475, 160 and 296 patients were diagnosed with USAP during the pre-pandemic, pandemic and post-pandemic periods, respectively.

The average number of cases diagnosed with STEMI and NSTEMI per month was significantly higher in the post-pandemic period than in the pre-pandemic and pandemic periods (p<0.001; Figure 1A and B). On the other hand, the average number of cases diagnosed with USAP per month was significantly lower during the pandemic and post-pandemic periods compared to pre-pandemic period (p<0.01; Figure 1C). However, the total number of ACS cases per month was significantly higher during the post-pandemic period than that during the pre-pandemic period (p<0.05, Figure 1D).

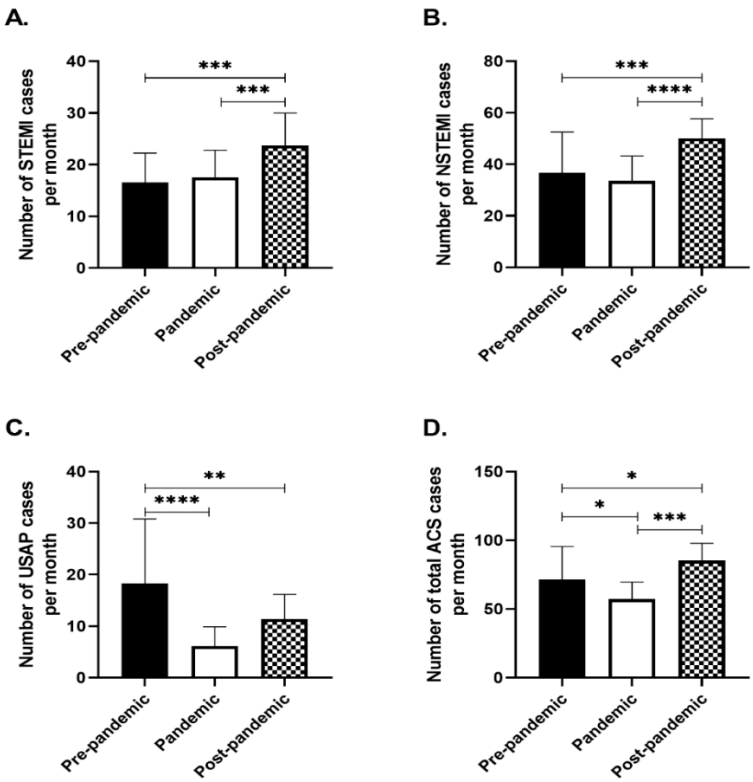

Figure 1. Number of **(A)** STEMI, **(B)** NSTEMI, **(C)** USAP and **(D)** total ACS cases per month during pre-pandemic, pandemic and post-pandemic periods (*p<0.05, **p<0,01, ***p<0,001 and ****p<0,0001; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; USAP, unstable angina pectoris; ACS, acute coronary syndromes).

The number of STEMI and NSTEMI cases showed a moderately positive correlation with time (Pearson r= 0.4823 and Pearson r= 0.4594, respectively; p<0.0001; Figure 2A and B), reflecting an increasing trend across the pre-pandemic, pandemic, and post-pandemic periods. However, there was no significant correlation between the number of USAP cases and time (Spearman r=−0.08669, p=0.4505, Figure 2C), indicating that the diagnosis of USAP did not vary across the pre-pandemic, pandemic, and post-pandemic periods. In contrast, a weak to moderate positive correlation was observed between the total number of ACS cases and time (Pearson r=0.3226, p=0.0040, Figure 2D). This trend suggests a gradual increase in ACS cases across the pre-pandemic, pandemic, and post-pandemic periods.

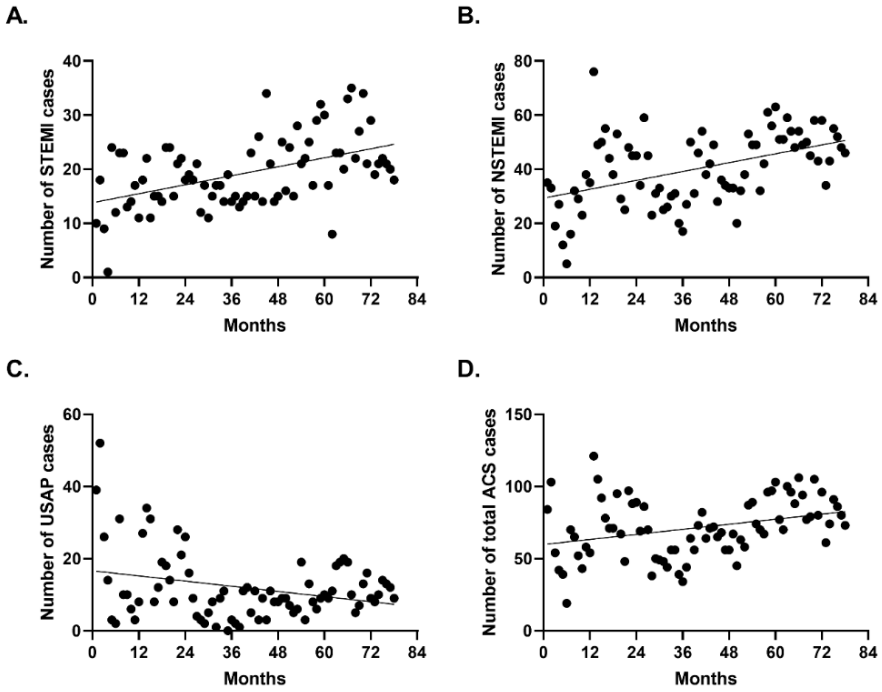

Figure 2. Number of **(A)** STEMI, **(B)** NSTEMI, **(C)** USAP and **(D)** total ACS cases throughout the study period. (STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; USAP, unstable angina pectoris; ACS, acute coronary syndromes)

Discussion

The present study represents a detailed retrospective evaluation of the temporal patterns of ACS across the pre-pandemic, pandemic, and post-pandemic phases of the COVID-19 era. The findings elucidate significant oscillations in ACS incidence, reflecting the intricate interrelation between the direct pathophysiological impacts of SARS-CoV-2 infection and the indirect consequences stemming from disruptions in healthcare delivery, public health infrastructure, and patient healthcare-seeking behaviors. These findings are critical for understanding the broader implications of global crises on cardiovascular health and identifying strategic targets for intervention.

The documented escalation in ACS cases, particularly STEMI and NSTEMI, during the post-pandemic phase lends robust support to the hypothesis that pandemic-induced delays in healthcare access exacerbated underlying cardiovascular risk profiles[22]. Fear of SARS-CoV-2 exposure and widespread healthcare system disruptions appeared to contribute significantly to this phenomenon, promoting disease progression and culminating in a rise in more severe ACS presentations during the post-pandemic period[23,24]. In a randomized study conducted by Soylu et al., it was found that the time STEMI patients continued to stay at home after the onset of chest pain during the pandemic period and the time to first admission to the hospital were considerably longer than in the pre-pandemic period. Door-to-balloon time and high procedural success were found to be similar in both periods[25]. Additionally, several societal and healthcare-related factors may help explain the observed rise in STEMI/NSTEMI incidence during the post-pandemic period. Following the initial phases of the COVID-19 pandemic, many healthcare centers resumed standard operations with enhanced safety measures, which likely alleviated concerns about seeking in-person treatment[26]. Concurrently, individuals who had postponed care during lockdowns or pandemic surges may have subsequently presented for catch-up diagnoses, contributing to an increase in recorded acute coronary events[27]. Additionally, successful vaccination campaigns and ongoing public health efforts may have improved patient confidence in hospital environments, further encouraging prompt medical attention for suspected cardiac symptoms[28,29]. Taken together, these developments likely converged to bolster healthcare engagement and reporting, thereby contributing to the increase in STEMI/NSTEMI incidence seen in the aftermath of the pandemic. Furthermore, the inflammatory milieu engaged by COVID-19, compounded

by endothelial dysfunction and a prothrombotic state, likely accelerated atherosclerotic processes, thereby amplifying the frequency and severity of MI[30-32]. These pathophysiological dynamics underscore the necessity of incorporating anti-inflammatory and endothelial-protective strategies into cardiovascular care frameworks, particularly during the post-pandemic recovery phase.In contrast to the significant fluctuations observed in STEMI and NSTEMI cases, the incidence of USAP remained relatively stable across the pre-pandemic, pandemic, and post-pandemic phases. This lack of significant variation may reflect the unique pathophysiology of USAP, which is frequently characterized by transient ischemic periods without the sustained myocardial necrosis observed in MI. It is plausible that patients experiencing USAP symptoms maintained similar healthcare-seeking behaviors across all phases, as the symptoms may not have been perceived as severe enough to evoke the same levels of pandemic-related care avoidance as seen in MI. Furthermore, the pathophysiological mechanisms driving USAP may be less influenced by the inflammatory and thrombotic effects of COVID-19, which appears to play a more substantial role in pathogenesis of STEMI and NSTEMI[33]. The relatively stable incidence of USAP highlights the need for further investigation into whether this subset of ACS represents a less sensitive to pandemic-induced disruption and how its management can be optimized during healthcare crises.

The temporal trends observed in this investigation provide critical insight into the persistent cardiovascular sequelae of the pandemic. The progressive rise in MI cases across the pre-pandemic, pandemic and post-pandemic phases likely reflects a multifactorial interplay of residual inflammatory and thrombotic effects associated with SARS-CoV-2 infection, disruptions in routine healthcare delivery, and delayed identification of preexisting cardiovascular pathologies[34,35]. These observations align with the extant literature underscoring the sustained adverse effects of pandemics on chronic disease trajectories, particularly in the cardiovascular domain. Moreover, the pandemic's-associated psychological and physiological stressors, including prolonged social isolation, economic uncertainties, and diminished physical activity, may have further exacerbated cardiovascular risk factors, potentiating the observed trends[36,37].

While the strengths including the reliance on a large dataset, several limitations must be acknowledged. The retrospective design inherently limits causal inference and introduces potential selection bias. Furthermore, the single-center focus restricts the generalizability of the findings, particularly across regions with differing healthcare infrastructures and pandemic responses. Future research should prioritize multicenter prospective studies to validate these findings and elucidate the underlying mechanisms with greater granularity. Additionally, there is imperative to identify and address the needs of populations disproportionately affected by pandemic-induced healthcare disruptions, through targeted interventions and resource allocation. Moreover, while our single-center design enabled us to collect comprehensive patient-level data under uniform protocols, we recognize that differences in local healthcare systems, pandemic response measures (e.g., timing and severity of lockdowns), and resource allocation could lead to variations in the incidence and management of acute coronary events in other regions. Moreover, demographic factors, public health policies, and levels of healthcare trust may differ markedly between geographic areas, potentially influencing patient behavior, such as willingness to seek care, and thus shaping observed outcomes. By acknowledging these region-specific factors, we underscore that our findings, although relevant, should be interpreted with caution when extrapolating to broader national or international contexts.

In conclusion, the findings of the present study highlight the profound and enduring impact of the COVID-19 pandemic on ACS presentation, extending well beyond its acute phase. These findings underscore the importance of embedding cardiovascular care into pandemic alertness strategies to avert comparable disruptions in future crises. Strengthening public health infrastructure, streamlining healthcare delivery, and enhancing chronic disease management are crucial for the mitigation of long-term cardiovascular sequelae of global health emergencies. Finally, the results suggest for the establishment of resilient, adaptive healthcare systems capable of ensuring continuity of care for both acute and chronic conditions amidst unprecedented challenges. Realizing these goals necessitates a multidisciplinary approach involving policymakers, clinicians, researchers, and community stakeholders, fostering the development of sustainable, equitable healthcare models that prioritize cardiovascular health within the broader context of global health security.

Compliance with Ethical Standards

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and approved by Amasya University Non-Interventional Clinical Research Ethics Committee (Date: 26 November 2024, No: 2024/123).

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

AC, OK: Study idea, hypothesis, study design, material preparation, data collection and analysis writing the first draft of the article, Critical review of the article finalization and publication process.

Financial Disclosure

None.

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