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PhD THESIS

**ADVANCED METHODS FOR PREDICTING THE
IMPACT OF CLIMATE CHANGE AND EXPOSURE
TO ATMOSPHERIC POLLUTANTS ON THE RISK
OF ACUTE CORONARY SYNDROME
OCCURRENCE**

ABSTRACT

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ABSTRACT

GENERAL PART

Cardiovascular disease (CVD), particularly acute coronary syndromes (ACS), remains the leading cause of morbidity and mortality worldwide, despite advancements in prevention and therapeutics. Although international data indicate a decreasing trend in cardiovascular morbidity and mortality, Romania reports a higher incidence and prevalence of ACS compared to many countries in Central and Western Europe.

In addition to the "classic" risk factors, growing evidence highlights the negative impact of air pollution and climate change on cardiovascular health. The major challenges of the modern era include increasing air pollution and global warming caused by industrial expansion, population growth, rapid economic development, and excessive energy consumption.

According to a recent report from "The Lancet," the average global temperature reached 1.14°C above pre-industrial levels between 2013 and 2022. If urgent action is not taken, it is estimated that by 2100, the global average temperature will reach a catastrophic 2.7°C.

The first evidence of the link between extremely low temperatures, industrial smog, and the incidence of acute cardio-respiratory diseases dates back to the early 20th century.

The general part of this work presents the latest information on the impact of air pollution and climate change on the risk of ACS, the latest data on the possible pathophysiological mechanisms of meteorological factors and atmospheric pollutants on atherosclerotic disease, and an overview of air pollution and CVD in the context of the COVID-19 pandemic.

The uncertainty regarding the pathophysiological mechanisms by which meteorological factors and atmospheric pollutants can trigger an acute coronary event, as well as the sometimes contradictory results from recent clinical and epidemiological research, has generated intense interest in the current theme of this paper. A detailed understanding of the relationship between the environment and the incidence of ACS is essential for implementing effective prevention measures, especially among vulnerable populations.

EXPERIMENTAL PART

1. OBJECTIVES AND DESIGN OF THE STUDY

CVDs are responsible for significantly reducing life expectancy and quality of life, generating enormous costs for health systems worldwide. The increase in air pollution and the global warming trend, driven by industrial expansion, population growth, rapid economic development, and excessive energy consumption, represent a significant threat to both the environment and cardiovascular health.

Epidemiological research in recent years has analyzed either the effect of the variation of meteorological factors on the risk of acute myocardial infarction (AMI), or the harmful impact of air pollution on the cardio-respiratory system, but few studies have examined the relationship between various atmospheric pollutants, climate change on short term and type of ACS (Acute ST-Elevation Myocardial Infarction - STEMI vs. Non-ST-Elevation Acute Coronary Syndrome - NSTEMI), especially among vulnerable populations. The study is an observational epidemiological investigation that analyzed the impact of acute exposure to air pollutants and short-term variations in meteorological factors on the risk of ACS with and without ST-segment elevation. The research was carried out within the Institute of Cardiovascular Diseases in Timișoara, and the objectives were achieved by conducting three main studies:

1. The first study included patients diagnosed with ACS with and without ST-segment elevation, analyzing the impact of short-term variations in meteorological factors (air temperature, atmospheric pressure, relative air humidity, wind speed, amount of precipitation, duration of sunshine and duration of cloudiness) on the risk of acute coronary events. Another objective of the research was to identify the categories of patients vulnerable to climate change, performing subgroup analyses according to the type of ACS (STEMI vs. NSTEMI), gender (men vs. women), and the presence of cardiovascular risk factors (CVRF - age ≥ 65 years, presence of diabetes mellitus - DM and arterial hypertension - HTN).

2. The second study included patients diagnosed with acute non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA), evaluating the impact of short-term exposure to elevated concentrations of atmospheric pollutants (Nitrogen dioxide - NO₂, Sulfur dioxide - SO₂, Ozone - O₃, Particulate matter with a diameter $\leq 10 \mu\text{m}$ - PM₁₀) on the risk of NSTEMI. The analysis was carried out both

on the whole group of patients and according to the type of ACS (NSTEMI vs. AI), season, gender, age (patients under 65 years vs. patients ≥ 65 years), the presence of CVRF (patients with and without DM, patients with and without HTN) and severity of coronary artery disease (CAD: single-vessel lesions and multi-vessel lesions).

3. The third study included patients diagnosed with STEMI, analyzing the relationship between short-term exposure to air pollution and the incidence of AMI according to seasonal variations in air pollutants. Subgroup analyses by age (young adults, middle-aged adults, and older adults) and gender were performed to identify potential differences in the effect of pollution on these subpopulations.

Next, the study results from the experimental part of the doctoral thesis are briefly presented.

2. SHORT-TERM CHANGES IN WEATHER CONDITIONS AND THE RISK OF ACUTE CORONARY SYNDROME HOSPITALIZATION WITH AND WITHOUT ST-SEGMENT ELEVATION: A FOCUS ON VULNERABLE SUBGROUPS

2.1. INTRODUCTION AND OBJECTIVES OF THE STUDY

In Romania, CVD accounts for more than half of the mortality rate, a figure almost twice that reported in the rest of Europe. However, data from the first Romanian registry for STEMI (RO-STEMI) show a decrease in the mortality rate of patients diagnosed with AMI from 13.2% in 2004 to 8.4% in 2009. Over time, numerous epidemiological studies have observed an increased incidence of AMI during the cold seasons in various geographic areas, such as Brazil, Germany, Australia, Japan, Portugal, France, and the USA. The present study aims to analyze the impact of short-term variations in meteorological factors on the risk of ACS, with and without ST-segment elevation, and to identify vulnerable subgroups. The results may help to understand the association between meteorological phenomena and the incidence of ACS, contributing to the development of plans aimed at mitigating the health impacts of climate change and reducing the costs of public health programs.

2.2. MATERIALS AND METHODS

This observational epidemiological study was conducted at the Institute of Cardiovascular Diseases in Timișoara, Romania, and included 5300 patients diagnosed with ACS between October 2016 and December 2021. The patients came from five counties in the country (Arad, Timiș, Caraș-Severin, Mehedinți, and Hunedoara) and were referred to the university hospital for coronary angiography. All adults admitted to the hospital were at least 18 years old and were diagnosed with either STEMI, NSTEMI, or unstable angina (UA). The study excluded minor patients, those diagnosed with chronic coronary syndrome (CCS), patients with AMI who died before or shortly after hospitalization without undergoing coronary angiography, individuals who did not provide informed consent, and those who had not resided in the geographical study area for at least one week before the onset of the acute coronary event.

The meteorological variables were provided by the National Meteorological Administration (NMA) of Romania. The data used in this study were collected from the weather station located in the patient's county of residence, where the patient had lived for at least seven days prior to the onset of the acute coronary event. The following meteorological factors were included: air temperature (minimum, maximum, and average values; °C), atmospheric pressure (minimum, maximum, and average values; mbar), relative air humidity (average value; %), precipitation (average value; mm/24 h), wind speed (maximum and average values; m/s), duration of sunshine (average value; h/day), and cloudiness duration (average value; h/day). These parameters were recorded as values starting on the day of hospitalization (day 0) and extending back to seven days before the onset of ACS (day 7). Subsequently, the variation of each parameter was determined for the seven days preceding the onset of AMI.

2.3. RESULTS

The study included 3504 patients (66.1%) diagnosed with STEMI and 1796 individuals (33.9%) hospitalized for NSTEMI-ACS. The average age of the hospitalized patients was 62.1 ± 11.5 years, with a higher prevalence of males (72.2%). Following coronary angiography, the majority of patients (38.5%) had single-lesion coronary artery disease, while only 120 participants (2.3%) had intact coronary arteries. The primary therapeutic approach was percutaneous coronary intervention (PCI) with stent

implantation (85.6%), followed by conservative treatment (9.1%). Surgical treatment (3.5%) and balloon angioplasty (1.8%) were used less frequently. Among patients diagnosed with STEMI, only 16.7% (884 individuals) received thrombolytic treatment prior to hospitalization.

Among elderly patients (≥ 65 years), 41.8% were hospitalized for STEMI, while 48% were diagnosed with NSTEMI-ACS ($p = 0.0036$). In the smoking patient cohort, 46.7% had STEMI at admission, while patients with DM (33.4% vs. 23.6%, $p < 0.001$) and HTN (87.2% vs. 64.5%, $p < 0.001$) were more prevalent in the NSTEMI-ACS group.

During the study period, the average number of admissions per day was 2.1 ± 1.2 cases. A single hospitalization per day was most frequently observed (59.91%), while in 3.92% of cases, there were four or more hospitalizations per day. The absence of admissions was observed on 2.91% of days. Most hospitalizations occurred in winter (December - February: 27.0%) and less often in spring (March-May: 22.7%).

An analysis of daily mean values of meteorological parameters according to ACS subtypes (STEMI vs. NSTEMI-ACS) revealed an increased incidence of admissions for STEMI on days with less sunshine, low temperatures, low atmospheric pressure, and high humidity compared to the number of NSTEMI-ACS cases.

A significant increase in the risk of ACS hospitalization was observed due to variations in air temperature, atmospheric pressure, sunshine duration, and cloudiness duration seven days prior to the onset of the acute coronary event. The daily number of hospitalizations for AMI increased by 5.9% for each 1°C variation in air temperature, by 2.4% for each 1 mbar change in atmospheric pressure, and by 4.7% and 3.9% for every 1-hour increase or decrease in sunshine duration and cloudiness, respectively. A modest but statistically significant relationship emerged between relative air humidity and ACS incidence, with each 1% change in air humidity increasing the risk of acute cardiac events by 0.5%. No statistically significant associations were identified between the risk of AMI and variations in wind speed and precipitation in the week before the onset of CVD. After excluding statistically insignificant meteorological variables, multiple regression analysis showed that the probability of an acute coronary event increases with greater variations in environmental factors one week before hospitalization.

The probability of having two hospitalizations per day for AMI is maximal when, 7 days before the cardiovascular event, there were fluctuations of 5°C in air temperature, 10 mbar in atmospheric pressure, 20% in air humidity, and variations of 5 hours in cloudiness and sunshine duration. These variations were considered reference threshold values, and the risk of at least two hospitalizations per day for ACS was

estimated accordingly. Short-term variations of $\geq 5^{\circ}\text{C}$ in air temperature and ≥ 10 mbar in atmospheric pressure increased the incidence of AMI by 55.2% and 58.7%, respectively. Additionally, the daily number of hospitalizations for ACS increased by 42.9% and 30.2% when the duration of sunshine and cloudiness varied by ≥ 5 hours in the previous week. A variation in air humidity of $\geq 20\%$ increased the risk of acute coronary events by only 18.4%.

To identify the categories of patients vulnerable to climate change, we performed a subgroup analysis according to gender (men vs. women) and the presence of CVRF (elderly patients - ≥ 65 years, hypertensive patients, diabetic patients) in the population diagnosed with STEMI and NSTEMI-ACS. Short-term climate change had a significantly greater impact on patients diagnosed with STEMI compared to those with NSTEMI-ACS. Variation in meteorological factors seven days before the onset of the cardiovascular event was associated with a significantly higher risk of STEMI in men compared to women. Male patients were much more sensitive to sudden changes in atmospheric pressure, leading to a 60% increase in the risk of hospitalization, while women showed greater vulnerability to atmospheric temperature fluctuations, which increased the incidence of AMI by 52%.

Variations in meteorological conditions determined a higher risk of AMI among elderly patients compared to diabetics and hypertensives. Changes in atmospheric pressure of at least 10 mbar increased the risk of hospitalization for STEMI by 63.2% among older adults, 57.4% in diabetic patients, and 61.4% in hypertensive patients. Similarly, temperature fluctuations of at least 5°C were responsible for increasing daily admissions for STEMI by 55.6% in the elderly, 48.3% in diabetics, and 54.4% in hypertensives. Variations in air humidity had a modest effect on the risk of STEMI, causing a 19.7% increase in daily hospitalizations among the elderly and 15.8% among hypertensive patients, with no statistically significant impact in the diabetic group.

3. IMPACT OF SHORT-TERM EXPOSURE TO NITROGEN DIOXIDE (NO₂) AND OZONE (O₃) ON HOSPITAL ADMISSIONS FOR NON-ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME

3.1. INTRODUCTION AND OBJECTIVES OF THE STUDY

In recent years, with increasingly evident climate changes due to global temperature rise, industrial expansion, and population growth, air pollution has become a significant threat to both the environment and human health. The WHO underscores the gravity of outdoor air pollution, attributing approximately 4.2 million premature deaths annually to it, 37% of which are caused by stroke and CVD. Additionally, the 2020 WHO report highlighted an estimated 3.2 million annual deaths due to household air pollution, noting that nearly a third of the global population still relies on inappropriate methods for heating and cooking, such as burning coal, wood, and agricultural waste. Major sources of outdoor pollution include agricultural practices, industrial activities, and transport, while indoor pollutants primarily stem from the burning of household fuels.

This study aims to evaluate the relationship between short-term exposure to increased concentrations of atmospheric pollutants—such as NO₂, SO₂, O₃, and PM₁₀—and the daily number of hospitalizations for NSTEMI-ACS. Statistical analyses were performed on the entire group of patients as well as subcategories according to season, gender, age, presence of CVRF, severity of coronary artery disease, and type of NSTEMI-ACS (UA vs. NSTEMI). The interaction between various meteorological factors and atmospheric pollutants was evaluated using Spearman correlation. Highlighting the negative impact of pollutants on acute coronary events can provide valuable information for implementing effective strategies to reduce pollution levels and, consequently, the risk to cardiovascular health.

3.2. MATERIALS AND METHODS

This observational epidemiological study was conducted at the Institute of Cardiovascular Diseases in Timișoara, Romania, and included patients hospitalized for NSTEMI-ACS from January 2019 to December 2021. Excluded from the study were minor patients, those diagnosed with STEMI, CCS, or other CVD, and those who had lived in the analyzed geographical area for less than two weeks.

Air pollutant data was obtained from the National Institute for Environmental Protection Research and Development. Data were collected from 24 fixed monitoring stations, with the selection of the pollution monitoring device situated in the closest proximity to the patient's residence. This paper included the daily average concentrations of NO₂, O₃, SO₂, and PM₁₀.

The meteorological variables analyzed were the average daily values of air temperature and relative humidity. These data were provided by NMA Romania and collected from fixed meteorological stations located in the county of each patient's residence. All meteorological and pollution data were recorded as daily mean values, starting on the day of hospitalization (day 0) and covering the seven days prior to the onset of the acute coronary event (day 7).

3.3. RESULTS

The study included a total of 1547 patients hospitalized for NSTEMI-ACS, with the majority diagnosed with UA (82.9%, 1283 patients), and 17.1% (264 patients) hospitalized for NSTEMI. The average age of the patients was 63.5 ± 10.0 years, and 48.5% of those hospitalized were over 65 years old. Men constituted 72.5% of the total study group. Among the patients, 86.7% were hypertensive, 38% had hypercholesterolemia, and 32.7% were diabetic. The primary therapeutic approach was primary PCI (84.4%), and 71.8% of patients had multi-vessel coronary artery disease.

During the study, the mean daily hospitalizations were 1.25 ± 0.91 . On most days, there was one hospitalization per day (47.9%), while in 9.1% of the period, there were 3 or 4 hospitalizations per day. Seasonal analysis revealed an increased frequency of 3 or 4 hospitalizations per day in the spring months, whereas summer saw one hospitalization per day in 54.5% of the study period.

We applied multivariable Poisson regression analysis to assess the association between days when air pollutants exceeded WHO recommended limits and the daily number of hospitalizations for NSTEMI-ACS. Statistical analysis was stratified by season, gender (men vs. women), age (<65 years vs. ≥ 65 years), type of CAD (single-vessel lesions vs. multi-vessel lesions), type of NSTEMI-ACS (NSTEMI vs. UA), and the presence or absence of CVFR (patients with DM vs. patients without DM; patients with HTN vs. patients without HTN). Air pollutants such as O₃ and SO₂, which exceeded the maximum concentration recommended by WHO on a limited number of days (0.52% for O₃ and 0.37% for SO₂), were also included in the statistical model for a more precise assessment of the influence of pollutants on the incidence of acute coronary events.

Seasonal analysis revealed that days when the mean NO₂ concentration exceeded the critical level of 25 µg/m³ were associated with a 22.3% increased risk of hospitalization for NSTEMI-ACS, regardless of the season (OR: 1.223, 95% CI 1.125–1.330; *p* < 0.001). The highest incidence of ACS was observed during spring, with a 42.6% increased risk of NSTEMI-ACS (OR: 1.426, 95% CI 1.196–1.710; *p* < 0.001), compared to summer days when the increase was 26.3% (OR: 1.263, 95% CI 1.072–1.487; *p* = 0.005).

In hypertensive patients, the risk of an acute coronary event increased by 10.1% on days with high NO₂ levels (OR: 1.101, 95% CI 1.007–1.204; *p* = 0.035). High NO₂ concentrations increased the risk of hospitalization for UA by 10.7% (OR: 1.107, 95% CI 1.010–1.213; *p* = 0.030) compared to cases of NSTEMI. No statistically significant results were observed in the analysis by gender, age, and type of coronary artery disease.

The impact of short-term increases (≥ 10 µg/m³) in air pollutant concentrations over various time intervals (0-3 days, 0-5 days, 0-7 days) on the daily number of hospitalizations for NSTEMI-ACS was analyzed according to different seasons. Each ≥ 10 µg/m³ increase in NO₂ level increased the risk of hospitalization for NSTEMI-ACS by 0.5% at 3 days (OR: 1.005, 95% CI 1.001–1.010; *p* = 0.017) and 5 days (OR: 1.005, 95% CI 1.000–1.009; *p* = 0.041) prior to the onset of the cardiovascular event, and by 0.6% 7 days before hospitalization (OR: 1.006, 95% CI 1.001–1.011; *p* = 0.010). Significant seasonal differences in ACS risk were observed. During spring, each 10 µg/m³ increase in NO₂ concentration was associated with a 1.3% increase in the risk of hospitalization for NSTEMI-ACS over the periods of 0-3 days (OR: 1.013, 95% CI 1.001–1.024; *p* = 0.027) and 0-7 days (OR: 1.013, 95% CI 1.001–1.025; *p* = 0.033), while in summer the risk increased by 1% for the 0-7 day period (OR: 1.010, 95% CI 1.001–1.019; *p* = 0.032). In winter, each 10 µg/m³ increase in O₃ level caused a 0.7% increase in the daily number of acute coronary events over 3 days (OR: 1.007, 95% CI 1.001–1.013; *p* = 0.029) and 5 days (OR: 1.007, 95% CI 1.001–1.014; *p* = 0.025) before hospitalization, with the greatest statistical impact observed in the 0-5 day period.

No statistically significant association was observed between elevated SO₂ or PM₁₀ concentrations and the risk of hospitalization for NSTEMI-ACS. This lack of association may be explained by the low levels of these pollutants in the geographical area studied.

4. SEASONAL VARIATION IN SHORT-TERM AMBIENT AIR POLLUTANTS AND ST-ELEVATION MYOCARDIAL INFARCTION ADMISSIONS: AN INNOVATIVE EXPLORATION OF AIR POLLUTION'S HEALTH CONSEQUENCES

4.1. INTRODUCTION AND OBJECTIVES OF THE STUDY

Numerous clinical and epidemiological studies have highlighted the detrimental health consequences of both long-term and short-term exposure to various environmental pollutants. These studies have confirmed the significant role of air pollution in triggering or exacerbating various CVDs, such as cardiac arrhythmias, decompensation of pre-existing heart failure (HF), and, notably, the incidence of ACS.

This research aimed to evaluate the impact of short-term seasonal variations in air pollutants on the risk of STEMI cases. Subgroup analyses were also conducted, considering age categories (young adults, middle-aged adults, older adults) and gender (male, female) to highlight potential differences in the effects of air pollutants within these subpopulations.

4.2. MATERIALS AND METHODS

This observational study included adults over 18 years old, diagnosed with STEMI at the Institute of Cardiovascular Diseases in Timișoara, Romania, between January 2019 and December 2021. Excluded from the research were patients under 18 years, those diagnosed with STEMI who died before or immediately after admission without undergoing coronary angiography, individuals diagnosed with UA or NSTEMI, participants who did not provide informed consent, and those who had not lived in the study area for at least two weeks.

Data on daily concentrations of atmospheric pollutants such as NO₂, PM₁₀, and O₃ were obtained from the Romanian National Air Quality Monitoring Network. These data were collected from 24 fixed monitoring stations located near the patients' residences. Meteorological factors, including relative air humidity and atmospheric temperature, were sourced from ANM Romania. This information was gathered from the day of the event to seven days prior to the onset of ACS. All meteorological and pollution variables were collected from the southwest region of Romania, a diverse geographical area with variations in meteorological parameters and air quality.

4.3. RESULTS

The observational epidemiological study included 2,570 patients diagnosed with STEMI. The majority of the study population were men (72.8%, 1,871 patients), while women were less represented (27.2%, 699 patients). The average age of hospitalized patients was 61.35 ± 12.17 years. Middle-aged adults comprised almost half of the study group (49.3%), followed by the elderly population (41.6%), and young adults (9.1%).

HTN was the most common comorbidity among patients diagnosed with STEMI (61.8%), with a smaller percentage having a history of DM (22.3%) or hypercholesterolemia (22.2%). Most patients with AMI had a single coronary artery lesion (45.2%) as diagnosed by coronary angiography. The main therapeutic approach was angioplasty with stent or balloon implantation (90.3%), and 23.3% received thrombolytic treatment before hospitalization.

The average number of admissions per day was 1.61 ± 0.81 , with one admission per day being the most common (69.7%). Two hospitalizations per day occurred 20% of the time, while 3 or more daily admissions occurred in 5% of cases. Zero admissions were observed on 5.3% of days. During the winter season, one hospitalization per day was observed on 71.7% of days, whereas during the summer, two or more hospitalizations per day were more common (28.2%).

Using multivariate Poisson regression analysis, the influence of air pollutants such as NO₂, PM₁₀, and O₃ on the daily number of hospitalizations for STEMI was assessed. The impact of rapid increases in air pollutant concentrations ($\geq 10 \mu\text{g}/\text{m}^3$) was examined for each individual day (from day 0, the day of admission, up to 7 days before the onset of ACS) and for combined periods of days (0-3 days, 0-5 days, 0-7 days).

Short-term increases in NO₂ concentrations had a significant impact on the daily number of admissions for STEMI during the spring season. This effect was observed from day 2 to day 3 and from day 6 to day 7 before hospitalization, with the most significant impact occurring one week after exposure to high NO₂ concentrations, leading to an increased risk of AMI by 0.8% (OR: 1.008, 95% CI: 1.002–1.014; $p = 0.014$). No other statistically significant correlations were observed between elevated NO₂ concentrations and the rate of hospitalization for STEMI in other seasons.

During summer, short-term increases in PM₁₀ concentrations significantly affected the daily incidence of ACS cases from day 0 to 7 days previously, with the strongest effect observed one week after exposure to high levels of the pollutant (OR: 1.017, 95% CI: 1.009–1.024; $p < 0.001$), resulting in a 1.7% increase in the incidence of STEMI. In the fall, high PM₁₀ concentrations significantly increased the risk of

STEMI from day 0 to 2 days before, reaching the maximum impact 1 day before hospitalization (OR: 1.006, 95% CI: 1.002–1.010; $p = 0.003$), leading to a 0.6% increase in daily admissions for ACS. No other statistically significant correlations were observed for the other seasons.

High levels of O_3 did not significantly affect the hospitalization rate for STEMI, likely due to the considerably lower concentrations of this pollutant in the studied geographic region.

Analysis of the entire study cohort revealed statistically significant cumulative effects for each $10 \mu\text{g}/\text{m}^3$ increase in NO_2 levels during the spring months. These effects were observed from 0-3 days to 0-7 days, with the most substantial impact seen at 0-7 days, resulting in a 0.9% increase in ACS admissions (OR: 1.009, 95% CI: 1.001–1.016; $p = 0.019$). During the summer, rapid increases in PM_{10} concentrations were associated with a heightened risk of hospitalization for STEMI from 0-3 days to 0-7 days, with a more pronounced effect at 0-7 days, leading to a 2.0% increase in hospitalization risk (OR: 1.020, 95% CI: 1.010–1.031; $p < 0.001$). During the fall, a sudden increase in PM_{10} concentration within the 0-3 day period was associated with a 0.6% rise in the risk of hospitalization for AMI (OR: 1.006, 95% CI: 1.001–1.011; $p = 0.011$). High O_3 concentrations did not show statistically significant cumulative effects on the hospitalization rate for STEMI in any season.

Subgroup analyses by gender (males and females) and age (young adults, middle-aged adults, and older adults) were conducted to assess the impact of pollutants on different patient categories. O_3 was found not to significantly affect AMI incidence in either individual day analyses or combined periods, leading to its exclusion from further subgroup analysis.

In the spring, men exhibited an increased risk of STEMI events following short-term rises in NO_2 concentrations, with the most significant effect observed at 0-7 days, resulting in a 1% increase in AMI incidence. No statistically significant impact of high NO_2 levels was noted among female patients. During the summer, PM_{10} had a significant effect on the male population, with the most notable impact at 0-7 days leading to a 2.1% increase in ACS admissions. Conversely, in the fall, the impact of PM_{10} on acute coronary events in men decreased, resulting in only a 0.6% increase in admissions within the 0-3 day period.

Regarding age, middle-aged and elderly adults demonstrated greater susceptibility to increases in NO_2 and PM_{10} concentrations compared to younger individuals aged 20 to 44, who did not show a statistically significant impact. Among middle-aged adults, elevated pollutant concentrations had the most significant cumulative effect at 0-7 days for both NO_2 in the spring and PM_{10} in the summer months. Particularly for PM_{10} , the highest impact was observed, resulting in a 2.0%

increase in the risk of coronary heart disease. For elderly adults, NO₂ exposure in the spring showed a cumulative effect from 0-3 days to 0-7 days, with the greatest impact observed at 0-3 days. PM₁₀ had the most significant effect on older adults during the summer, particularly at 0-7 days when the risk of STEMI increased by 1.9%. In the fall, high levels of PM₁₀ during the 0-3 day period led to a 0.7% increase in AMI cases.

CONCLUSION

The impact of climate change and exposure to atmospheric pollutants on the risk of ACS was the primary focus of the three original studies presented in the Experimental Part of the doctoral thesis. The objectives of the doctoral thesis were achieved through these studies, each contributing to a deeper understanding of how climate change and air pollution affect the incidence of ACS.

Upon completing the doctoral thesis, the following **conclusions** were drawn:

1. Meteorological parameters, particularly short-term variations in atmospheric pressure and air temperature, significantly influence the incidence of ACS.
2. Short-term fluctuations in meteorological factors were associated with a higher probability of STEMI cases compared to NSTEMI-ACS.
3. Men and individuals over the age of 65 were more susceptible to short-term climate changes compared to younger subjects and women.
4. Increased emissions of atmospheric pollutants, such as NO₂ and O₃, were associated with a higher probability of NSTEMI-ACS cases, especially in certain seasons.
5. During spring, exposure to high concentrations of NO₂, above the WHO-recommended limits, significantly increased the risk of hospitalization for NSTEMI-ACS. The harmful impact of NO₂ was particularly observed among hypertensive patients and those diagnosed with UA.
6. High concentrations of NO₂ in spring and O₃ in winter increased the risk of hospitalization for NSTEMI-ACS by 1.3% and 0.7%, respectively.

7. The association between daily admissions for ACS and air pollution was more pronounced when considering the cumulative effect of pollutants over time rather than focusing on any single lag day.
8. High levels of NO₂ during spring and PM₁₀ during summer and fall were associated with a significant increase in hospitalizations for STEMI. The most statistically significant effect was observed 7 days after exposure to NO₂ in spring, and 3 and 7 days after exposure to high concentrations of PM₁₀ in summer and autumn.
9. The harmful impact of NO₂ and PM₁₀ was particularly observed among men and adults over 45 years diagnosed with STEMI, compared to women and younger individuals.

This research stands out due to the following **original contributions**:

- Identifying the importance of short-term weather variations as predictors of the risk of ACS, especially STEMI.
- Documenting a seasonal relationship between high levels of NO₂ and O₃ and the risk of hospitalization for NSTEMI-ACS.
- Identifying significant seasonal variations in the harmful effects of air pollution on the risk of STEMI cases.
- Men and adults over 45 are more susceptible to climate change and air pollution than women and the younger population, emphasizing the importance of demographic factors in assessing vulnerability.

Future research directions are:

- Conducting studies on larger groups of patients and in varied geographical areas to confirm the results obtained.
- Investigating the long-term impact of air pollution and weather variations on cardiovascular health.

- Evaluating the impact of several atmospheric pollutants, such as SO₂, PM_{2.5}, and ultrafine particles (UFP), on the incidence of ACS, and analyzing the combined effect of these factors.
- Investigating the impact of population exposure to indoor environmental pollutants and their correlation with clinical data.
- Identifying the biological and pathophysiological mechanisms underlying the relationship between climate change, air pollution, and the incidence of ACS to determine the most effective preventive measures.