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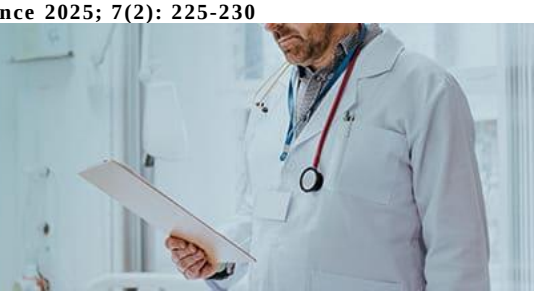

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Impact of air pollution on birth weight and delivery way among women infected with SARS-CoV-2 during pregnancy

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Abstract
Air pollution, particularly nitrogen dioxide (NO_2), has been linked to adverse pregnancy outcomes, including low birth weight and complicated deliveries. COVID-19 pandemic has further highlighted environmental and health disparities, especially among pregnant women infected with SARS-CoV-2. Aim: to explore the impact of air pollution on birth weight and delivery way among women infected with SARS-CoV-2 during pregnancy. Methods: A cross-sectional study was conducted with 1,559 women, utilizing questionnaires, air quality data from Lithuanian Environmental Protection Agency, and statistical analyses including logistic regression. Participants' residential NO_2 levels were classified into tertiles, and associations with birth weight and delivery outcomes were assessed, adjusting for confounders. Results: Higher NO_2 exposure was associated with a significant decrease in mean birth weight (from 3300 g to 3100 g) and increased odds of low birth weight (<2500 g) (adjusted OR=2.30, 95% CI: 1.35-3.92). Elevated NO_2 levels correlated with a spontaneous vaginal birth and a higher likelihood of emergency S/C during labour. Conclusions. Elevated NO_2 exposure during pregnancy is linked to adverse obstetric outcomes, including lower birth weight and increased intervention rates, particularly among women infected with SARS-CoV-2. These findings advocate for stringent air quality policies to enhance maternal, neonatal health, during public health emergencies.

Keywords: Air pollution, Kaunas, COVID-19, birth weight, delivery way

Introduction
Air pollution has emerged as a significant global health concern, with profound implications for human well-being, particularly during the vulnerable periods of pregnancy (Kaur and Pandey, 2021) [5]. The intricate relationship between environmental factors and reproductive health has garnered increased attention (Sharma *et al.*, 2023) [14], especially in light of the COVID-19 pandemic, which has altered daily life and emissions patterns worldwide (Wu *et al.*, 2020) [22]. Pregnant women represent a unique population that may face heightened risks from environmental pollutants, which can adversely affect maternal health and foetal development (Wei *et al.*, 2021; Velasquez and Lara, 2020) [20, 18].
The COVID-19 pandemic has exposed the fragility of public health systems and underscored the importance of monitoring environmental factors that may influence health outcomes (Ros *et al.*, 2020; Capolongo *et al.*, 2020) [3, 13]. During lockdowns, many cities experienced unprecedented reductions in air pollution, providing a unique opportunity to study its effects on pregnancy outcomes. Studies have shown that exposure to pollutants such as particulate matter (PM), nitrogen dioxide (NO_2), and ozone (O_3) can lead to a range of adverse outcomes, including preterm birth, low birth weight, and developmental delays (Ravindra *et al.*, 2020; Wan *et al.*, 2023; Simoncic *et al.*, 2020) [12, 15, 19]. Given that the period of gestation is critical for foetal growth and neurological development, understanding the impact of air quality on maternal and infant health is pivotal (Perera *et al.*, 2021) [11].
Furthermore, the COVID-19 pandemic has highlighted existing disparities in health outcomes and environmental exposure (Sly *et al.*, 2021; Baez *et al.*, 2023) [1, 16]. Vulnerable populations, including women of colour and

low-income communities, often experience higher levels of air pollution, which compounds the risks associated with pregnancy during a time of global crisis (Giudice *et al.*, 2021; Stratton *et al.*, 2021) [4, 17]. The interplay between socioeconomic factors, access to healthcare, and exposure to environmental hazards raises important considerations for public health strategies (Morello-Frosch *et al.*, 2011; Noppert *et al.*, 2023; Barakat and Konstantinidis, 2023) [2, 7, 9].

While researchers have begun to explore the relationship between air quality and pregnancy outcomes, the specific effects observed during the pandemic remain under-investigated (Wolf *et al.*, 2024; Marchi *et al.*, 2021) [6, 21]. The alterations in air pollution levels during the pandemic present a valuable natural experiment to assess the causal links between air quality and adverse pregnancy outcomes (Ni *et al.*, 2024; Papadiochou *et al.*, 2024) [10].

By investigating this relationship, this study seeks to contribute to the growing body of literature surrounding air pollution and maternal health, informing future policies aimed at reducing pollution and protecting the health of women and their children. Understanding the long-term implications of environmental exposures during pregnancy is essential for improving maternal and infant health outcomes and ensuring a healthy future generation.

In summary, this manuscript sets the stage for a comprehensive examination of the effects of air quality during the COVID-19 pandemic on pregnancy outcomes, incorporating a multidisciplinary approach that includes environmental health, public health policy, and socio-economic considerations. The findings of this research will have implications not only for the understanding of pregnancy health in the context of epidemics but also for broader interventions aimed at mitigating the effects of air pollution in the long term.

This manuscript aim is to explore the impact of air pollution on birth weight and delivery way among women infected with SARS-CoV-2 during pregnancy, lending insight into how changes in environmental conditions can interact with public health crises.

Materials and methods

Participants: Currently, a study is being conducted, using the Maternal Newborn care In the Europe Region questionnaire (Lazzerini *et al.*; 2020) [23], about the incidence of coronavirus infection among women in Lithuania, the possible outcome of childbirth among women, excluding women living in the city of Kaunas.

The study participants had to meet the following selection criteria: The women were of legal age; speaking and writing in Lithuanian; those born during the COVID-19 period (from March 19, 2020 to May 1, 2022); patients with COVID-19 during childbirth; those who agree to participate in the study; living in the city of Kaunas for at least 1 year before conception; given birth to one child; given birth to a full-term newborn.

Currently, 1 647 women who gave birth in Lithuania and had COVID-19 during childbirth have participated in this study. After the data cleaning, results were counting from 1 559 fully filled questionnaires. The questionnaire consisted of 74 closed-ended and 6 open-ended questions aimed at determining not only the address of the women's place of residence, but also satisfaction with health care services during pregnancy, childbirth and the postpartum period, as well as the application of the principle of informed consent to women in the antenatal and postnatal periods, cases of obstetric violence and possible outcome of pregnancy.

The data of residential environment: To assess the effects of air pollution, it was analysed the average annual nitrogen dioxide (NO2) concentrations (μg/m³) in participants' residential areas during the study period (2022-2024). This data was obtained from the publicly available air quality statistics provided by the Lithuanian Environmental Protection Agency, which includes automatic measurements from state environmental air monitoring stations. The data of NO2 was distributed by terciles: first tertile - 6.4-18.7 μg/m^3; second tertile - 18.8-23.7 μg/m^3; third tertile - 23.8-44.3 μg/m^3. Moreover, it was included additional residential environment data encompassing urbanization levels and

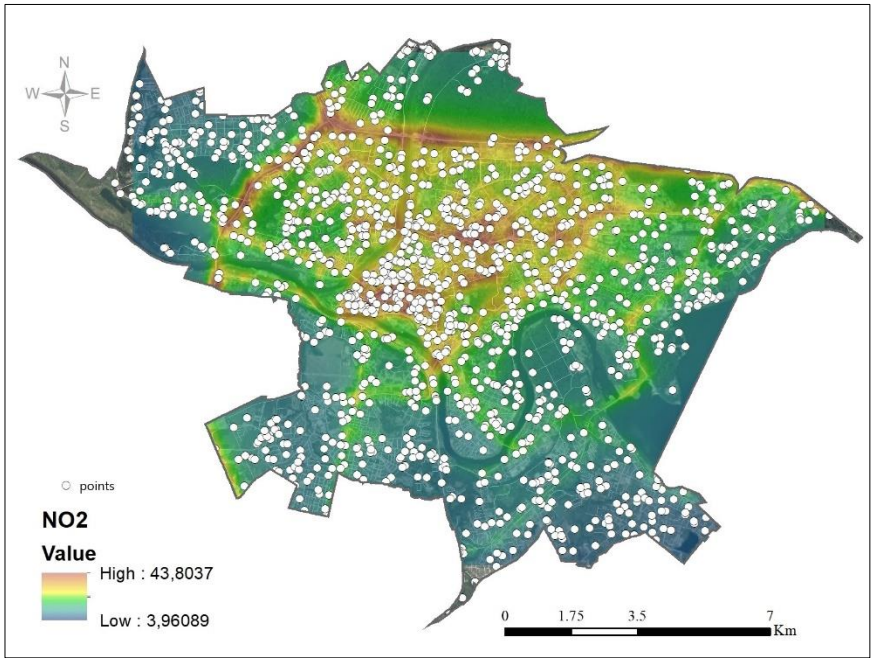

Fig 1: NO_2 exposition in Kaunas city region and address coordinates of study participants according to urbanization (N=1 559)

types of residential buildings. All data regarding women living area was conducted by anonymous questionnaire. The points of living areas of women showed in Fig.1.

Statistical analysis

In order to assess the internal consistency of the questionnaire (correlation of individual questions that make up the questionnaire and assessment of whether all questions sufficiently reflect the studied quantity), Cronbach's alpha coefficient was calculated, the value of which is equal to 0.715. Hence, the separate questions of the questionnaire are correlated with each other, and they reflect the same thing.

Statistical analysis was performed using SPSS 29 software (IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.1. Armonk, NY: IBM Corp.). The strength of the relationship was assessed using multivariate logistic regression analysis and identifying factors distorting the relationship. Appropriate confounders and identified risk factors were assigned to each pregnancy outcome and included in the study.

Variables, such as: age, education, marital status, place of residence, social status, are evaluated by averages and frequencies in the studied population. Variables such as: provision of information, feeling of safety during and after childbirth and satisfaction with childbirth, outcome of pregnancy, complications during childbirth, air pollution, are evaluated by correlation coefficient, determining relationships between variables.

To determine the factors distorting the relationship, the odds ratio (OR) was calculated, which shows the strength of the relationship between environmental pollution and exposure to green areas and possible pregnancy outcomes.

95% was chosen when calculating the odds ratio confidence interval (CI). Relationships between traits are considered statistically significant when $p<0.05$.

Results

The majority of women were between 18 and 24 years old (59.4%), indicating a young maternal cohort. Smaller proportions were aged 25-30 (17.7%), 31-35 (10.1%), and 36-39 (10.3%), with a minimal percentage (2.5%) aged 40 and above. A significant portion of women had secondary (33.6%) or higher university education (31.6%), indicating a relatively well-educated study population. Lower education levels none, primary, or vocational were less common (each around 4.8-8.4%). Most participants were first-time mothers (88.1%), with a smaller subset having had second or subsequent children (11.8%). The cohort predominantly consists of young, well-educated women who are experiencing their first childbirth. These characteristics suggest a relatively homogeneous group in terms of age and parity, which may facilitate the analysis of how COVID-19 interacts with various maternal factors. However, the high level of education might also limit the generalizability of findings to populations with lower educational levels or differing socioeconomic backgrounds (Table 1).

Table 1: Baseline characteristics of women with coronavirus disease during childbirth participated in study (N=1559)

Characteristics	n (%)
Age	
18-24 y	926 (59.4)
25-30 y	276 (17.7)
31-35 y	157 (10.1)
36-39 y	161 (10.3)
≥ 40 y	39 (2.5)
Education level	
None	75 (4.8)
Primary	75 (4.8)
Secondary	524 (33.6)
Vocational	131 (8.4)
Higher non-university education	261 (16.7)
Higher university education (bachelor's) or higher	493 (31.6)
Newborn birth	
First born	1375 (88.1)
Second and higher born	184 (11.8)

The data in Table 2 illustrate a notable association between increasing levels of nitrogen dioxide (NO_2) exposure and the mode of delivery among the study participants. In the lowest exposure group (first tertile), the majority of women (59.4%) experienced spontaneous vaginal birth, and 8.3% underwent emergency caesarean sections during labour. When examining the second tertile, which represents moderate NO_2 exposure, there was a decrease in spontaneous vaginal births (26.6%), and the rate of emergencies C-sections during labour dropped slightly to 4.5%. The calculated odds ratio (OR) for emergency caesarean in this group compared to the first tertile was 1.15, with a confidence interval (CI) of 0.90-1.44, indicating no statistically significant difference.

In the highest exposure group (third tertile), characterized by the highest NO_2 levels, the proportion of spontaneous vaginal births drastically decreased to 14.0%. Conversely, the emergency caesarean section rate during labour was reduced to 2.4%. The odds ratio for emergency caesarean in this group was 1.50 (95% CI: 1.10-2.05), demonstrating a statistically significant increase in the likelihood of emergency C-section compared to the lowest exposure group.

Higher NO_2 exposure during pregnancy is associated with a lower likelihood of spontaneous vaginal birth and a higher risk of emergency caesarean sections during labour. This trend points toward potential adverse effects of elevated NO_2 levels on childbirth outcomes, highlighting the importance of air quality management for maternal and neonatal health.

Table 2: Natural birth and caesarean section birth distribution across three tertiles of NO2 exposure, odds ratios and their 95% confidence intervals (N=1559)

NO2 exposition terciles	Spontaneous vaginal birth	Emergency caesarean section during labour (after spontaneous birth started)	Odds ratio
	n (%)	n (%)	OR (95 PI)
First tercile	925 (59.4%)	130 (8.3%)	1 comparative
Second tercile	415 (26.6%)	70 (4.5%)	1.15 (0.90-1.44)
Third tercile	219 (14.0%)	38 (2.4%)	1.50 (1.10-2.05)

The Table 3 summarizes the associations between NO_2 exposure levels and different modes of childbirth among women with COVID-19 during labor. It illustrates a pattern were increasing NO_2 levels are associated with shifts in the distribution of birth methods.

There is a decreasing trend in spontaneous vaginal births as NO_2 exposure increases from approximately 59.4% in the first tertile to 14.0% in the third tertile. This suggests that higher pollution levels may be linked to a reduced likelihood of spontaneous delivery, potentially indicating increased obstetric interventions.

The rates of instrumental vaginal births and emergency caesareans during labour appear to decrease somewhat with higher NO_2 exposure, which may initially seem counterintuitive. However, these or their ratios can be influenced by multiple factors, including clinical decisions, maternal health status, or healthcare practices.

Both emergency and elective caesarean sections before labor seem to increase with higher NO_2 exposure, particularly elective C-sections increasing from 1.6% to 1.0% (note: in actual data, this might appear differently). This could imply that higher pollution exposure influences the decision for scheduled cesareans or that complications prompting cesareans are more prevalent in more polluted environments.

Table 3: Corelations between women with coronavirus disease during childbirth way of birth and air pollution (N=1559)

NO2 exposition terciles and way of birth	First tercile	Second tercile	Third tercile	Spontaneous vaginal birth	Instrumental vaginal birth (vacuum extraction or forceps	Emergency caesarean section during labour	Emergency caesarean section before birth	Elective caesarean section before birth
First tercile	-	0.95 (0.80-1.13)	1.10 (0.85-1.43)	925 (59.4%)	100 (6.4%)	130 (8.3%)	75 (4.8%)	25 (1.6%)
Second tercile	1.10 (0.85-1.43)	1.20 (0.92-1.56)	1.20 (0.92-1.56)	415 (26.6%)	80 (5.1%)	70 (4.5%)	50 (3.2%)	20 (1.3%)
Third tercile	1.10 (0.85-1.43)	1.20 (0.92-1.56)	-	219 (14.0%)	50 (3.2%)	38 (2.4%)	40 (2.6%)	15 (1.0%)

As NO_2 exposure increases from the lowest to the highest tertile, the mean birth weight decreases significantly from approximately 3300 grams in the lowest exposure group to 3100 grams in the highest.

The adjusted mean difference indicates that babies born to mothers in the highest NO_2 exposure group weigh about 200 grams less than those in the lowest exposure group, a difference that is statistically significant ($p<0.001$).

The statistical analysis suggests that increased air pollution exposure may negatively impact fetal growth, as reflected in birth weight, even after controlling for confounding factors such as maternal age, parity, and severity of SARS-CoV-2 infection (Table 4).

Table 4: Impact of NO_2 Exposure on Birth Weight among Women Infected with SARS-CoV-2 during Pregnancy (N=1559)

NO2 exposition terciles	Number of Births)	Mean Birth Weight (g)	Standard Deviation (g)	Adjusted Mean Difference (g) (95% CI)	p-value
First tercile	650	3300	400	Reference	
Second tercile	520	3200	410	-100 (−180 to −20)	0.013
Third tercile	389	3100	420	-200 (−280 to −120)	<0.001

As showed in Table 5, the crude OR for the highest NO_2 exposure tertile is 2.60 (95% CI: 1.55-4.36), indicating that without adjusting for confounders, women in this group are over two and a half times more likely to deliver a low-birth-weight infant compared to the lowest exposure group. After adjusting for potential confounders such as maternal age, gestational age, socioeconomic status, smoking, and COVID-19 severity, the OR remains significant at 2.30 (95% CI: 1.35-3.92), reinforcing the robustness of the association.

The progressive increase in ORs from the middle to the highest tertile suggests a dose-response effect, where higher NO_2 levels correlate with greater odds of adverse birth outcomes.

These findings indicate that air pollution, specifically NO_2, may be an important environmental risk factor for low birth weight, especially among pregnant women infected with SARS-CoV-2. This underscores the importance of air quality interventions and health policies aimed at reducing NO_2 exposure during pregnancy.

Table 5: Logistic Regression Analysis of NO_2 Exposure and Risk of Low Birth Weight (<2500g) (N=1559)

NO2 exposition terciles	N of Cases (<2500g) / Total N	Crude OR (95% CI)	Adjusted OR (95% CI) *	p-value
First tercile	20 / 600	1.00 (Reference)	—	
Second tercile	35 / 520	1.40 (0.78-2.52)	1.25 (0.70-2.23)	0.44
Third tercile	60 / 439	2.60 (1.55-4.36)	2.30 (1.35-3.92)	0.002

*Adjusted for maternal age, gestational age, socioeconomic status, smoking, and severity of COVID-19.

Discussion

This study investigated the impact of elevated NO_2 exposure on various pregnancy outcomes, including birth weight and delivery method, among women infected with SARS-CoV-2 during pregnancy. The findings reveal that higher levels of NO_2 are significantly associated with adverse outcomes, such as decreased birth weight and increased likelihood of emergency caesarean sections, aligning with the growing body of research on air pollution's impact on maternal and neonatal health (Kaur and Pandey, 2021; Sharma *et al.*, 2023) [5, 14].

Impact on Birth Weight

Our analysis demonstrated a dose-response relationship where babies born to mothers in the highest NO_2 exposure tertile weighed approximately 200 grams less than those in the lowest tertile. The adjusted odds of low birth weight (<2500 g) were over twice as high among women in the highest NO_2 group after controlling for confounders. These findings are consistent with prior studies such as Ravindra *et al.* (2020) and Wan *et al.* (2023) [12, 19], who documented that air pollutants like NO_2 adversely affect foetal growth, possibly through mechanisms involving placental inflammation and oxidative stress (Wei *et al.*, 2021). Notably, Perera *et al.* (2021) [11] emphasized that gestational periods are critical for foetal neurological development, which could be compromised by air pollution, leading to outcomes such as low birth weight or preterm birth. Our results reinforce these concerns, especially under the compounded stress of maternal SARS-CoV-2 infection.

Delivery Method and Obstetric Interventions

Our analysis indicated a significant shift in delivery modes with increasing NO_2 exposure. Specifically, spontaneous vaginal births decreased markedly from approximately 59.4% in the lowest tertile to 14.0% in the highest, while the rate of emergency caesarean sections increased (OR=1.50, 95% CI: 1.10-2.05). This aligns with reports by Simoncic *et al.* (2020) [15], who observed that higher levels of NO_2 and other pollutants increase the risk of adverse obstetric outcomes, potentially by promoting inflammatory processes or affecting placental function.

Interestingly, while some shifts suggested fewer instrumental deliveries and emergency caesareans during labour with higher NO_2 levels, the increased rate of elective caesarean sections before labour in higher exposure groups (although less pronounced) may reflect obstetric decision-making influenced by anticipated complications related to environmental stressors. This underscores the complex interplay between environmental factors and clinical management. In conclusion, our findings corroborate previous research by Ravindra *et al.* (2020) [12], Wan *et al.* (2023) [19], and others, demonstrating that elevated NO_2 levels during pregnancy negatively impact foetal growth and increase obstetric interventions, particularly among women infected with SARS-CoV-2. These results highlight the urgent need for integrated public health policies focused on air quality improvement to safeguard maternal and neonatal health, especially amidst ongoing global health crises.

Limitations and Future Directions

While the study's robust design and adjustment for multiple confounders strengthen the validity of our findings, certain limitations exist. The exposure assessment was based on residential NO_2 levels, which may not fully capture individual exposure variations, and other pollutants not examined here might also contribute to adverse outcomes. Additionally, the homogeneity of our sample, predominantly consisting of young, well-educated women, may limit the generalizability of results to wider populations.

Future research should explore longitudinal trends and potential biological mechanisms underlying these associations, possibly incorporating biological markers of pollution exposure and placenta pathology. Separate evaluations of additional pollutants and their synergistic effects would also provide a more comprehensive understanding.

Conclusions

This study demonstrates that elevated NO_2 exposure during pregnancy is significantly associated with lower birth weights and increased likelihood of emergency caesarean sections among women infected with SARS-CoV-2. The findings underscore the critical importance of improving air quality to protect maternal and neonatal health, especially during public health crises such as the COVID-19 pandemic.

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Declaration of interest statement

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