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Women with preeclampsia exposed to air pollution during pregnancy: Relationship between oxidative stress and neonatal disease - Pilot study

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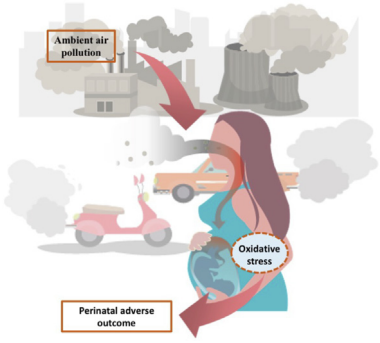
HIGHLIGHTS

- Exposure to air pollution induces to oxidative damage and adverse perinatal outcome.
- Critical windows of early exposure in preeclamptic pregnancy are identified.
- Neonatal diseases are associated with pregnancies that develop preeclampsia.
- There is a correlation between oxidative stress markers levels and neonatal diseases.

GRAPHICAL ABSTRACT



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ABSTRACT

Oxidative imbalance as a pathophysiological mechanism has been reported as an adverse outcome in pregnant women who develop preeclampsia and in their newborns. Furthermore, emerging evidence suggests the same mechanism by which air pollutants may exert their toxic effects. Therefore, the objective of the study was to evaluate the biomarkers of oxidative stress and their relationship with neonatal disease in premature newborns from mothers with preeclampsia exposed to air pollution during pregnancy. The data of air pollutants ($PM_{2.5}$, PM_{10} and ozone) were collected at fixed monitoring stations. Oxidative and antioxidant status markers were obtained through special techniques in women with preeclampsia and in umbilical cord blood of their premature newborns. The oxidative stress markers were significantly higher in women with preeclampsia and their newborns who were exposed to higher levels of ambient air pollutants in the first and second trimester of pregnancy. Neonatal diseases are associated with preeclampsia in pregnancies, specifically intrauterine growth restriction (IUGR) and necrotizing enterocolitis (NEC). A significant correlation was identified in the levels of prooxidant agents and antioxidant enzyme activity in the presence of neonatal diseases associated with preeclampsia. There is increased oxidative damage in both the maternal and fetal circulation in women who develop preeclampsia exposed to air pollution during pregnancy. Therefore, these pregnancies complicated by preeclampsia have a greater adverse outcome as neonatal disease in the preterm infant.

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1. Introduction

Pregnancy is a condition that requires a higher ventilation rate and tidal volume due to the increased oxygen requirements of the developing fetus (Soma-Pillay et al., 2016). This makes pregnant women vulnerable to the effects of air pollution. Fine particles matter with an aerodynamic diameter <2.5 μm and <10 μm ($PM_{2.5}$ and PM_{10}) and ozone (O_3), allow their passage through the maternal respiratory tract and their entry into the blood circulation. The mechanisms described by which exposure to air pollutants exert their toxic effects are an inflammatory process and oxidative stress (OS) (Jia et al., 2017; Kim et al., 2015; Pedersen et al., 2014). This leads to adverse perinatal outcomes such as preterm delivery, low birth weight, fetal growth restriction (Fu et al., 2019), and hypertensive disorders during pregnancy such as preeclampsia (Dadvand et al., 2014; Pereira et al., 2013). Some studies have reported an association between preeclampsia and maternal exposure to gaseous components of air pollution such as ozone and particulate matter in both low and high exposed areas (Pedersen et al., 2017; Wang et al., 2018).

Preeclampsia is a hypertensive disorder associated with pregnancy; an incidence of 5 to 15 % of all pregnancies is reported, resulting in high fetal or maternal morbidity and mortality (Schoots et al., 2018; The American College of Obstetricians and Gynecologists, 2019). Pathophysiological changes with the presence of high levels of OS as well as a generalized inflammatory state are characteristic of preeclampsia. Placental oxidative stress resulting from ischemia-reperfusion injury is involved in the pathogenesis of this prenatal syndrome (Pimentel et al., 2013; Schoots et al., 2018). It is observed a significant increase in lipid peroxidation and malondialdehyde levels in the placenta of preeclamptic women (Duhig et al., 2016). These mechanisms could be influential variables for the risk of damage by reactive oxygen species (ROS) in newborns from preeclamptic/eclamptic pregnancies (Buonocore et al., 2017). OS has been implicated in the development and pathogenesis of several diseases in newborns and especially in premature newborn, are very susceptible to oxidative damage. (Gitto et al., 2013; Ozsurekci and Aykac, 2016; Perrone et al., 2012). Numerous researches have shown that oxidative stress is implicated in the pathogenesis of serious neonatal diseases, the “oxygen radical diseases in neonatology”; which translates to the fact that oxidative stress affects a variety of organs, often simultaneously, and gives rise to different signs according to the most damaged organ, causing neonatal diseases (Marseglia et al., 2014; Negi et al., 2014; Ozsurekci and Aykac, 2016; Perrone et al., 2012).

Therefore, particulate matter and atmospheric gases-induced oxidative stress during pregnancy may alter placental vascular function, the development of preeclampsia in an adverse intrauterine environment and affect fetal development and growth. Although free radical injury is identified in the pathogenesis of neonatal disease, it is necessary to establish a clear definition of its degree of participation and the early identification of newborns at risk of oxidative stress. Therefore, the aim of the study was to evaluate the biomarkers of oxidative stress and their relationship with neonatal disease in premature newborns from mothers with preeclampsia exposed to air pollution during pregnancy.

2. Material and methods

2.1. Site sampling technique

The Metropolitan Zone of the Valley of Toluca (MZTV) is an area of 2669.6 km^2. The MZTV has a vehicular fleet of 430,000 vehicles and 2.1 million inhabitants and is considered one of the largest urban areas heavily polluted in Mexico. It is surrounded by rural and suburban municipalities.

The MZTV has a network of air quality monitoring six stations known locally as the Red Automática de Monitoreo Ambiental de Toluca (RAMAT) – To the North San Cristóbal Huichochitlán (SC), East San Mateo Atenco (SM), South Ceboruco Station (CB) and Metepec (MT), West San Mateo Oxtotitlán (OX) and Center (CE). These monitoring stations are classified into three zones: Center (San Mateo Oxtotitlán), North (San Lorenzo Tepaltitlán, San Cristóbal Huichochitlán and Aeropuerto) and South (Metepec and San Mateo Atenco) (Romero-Guzmán et al., 2018) (Fig. 1).

2.2. Exposure estimates

Air pollutant data ($PM_{2.5}$, PM_{10} and O_3) were collected from February 2017 to February 2019. Measurements from the 6 fixed monitoring stations of air pollution from the Red Automática de Monitoreo Ambiental de Toluca (RAMAT) were used (available in https://rama.edomex.gob.mx). The analysis methods for contaminants have official methodologies established as standards for measurement and analysis considered as international criteria. Attenuation of Beta Radiation is used to quantify the concentration of Suspended Particles of respirable fraction PM_{10} and $PM_{2.5}$. It is a federal equivalent method (FEM) for the continuous monitoring of particles, certified by the USEPA (United States Environmental Protection Agency). Ultraviolet Absorption Spectrometry is used to measure the ozone concentration in the air. Criteria to discern the origin of the elements was based on the main characteristics of monitoring stations surroundings such as traffic, the presence of factories, population density, location and inhabited areas nearby. The exposures were assigned using the monitoring station nearest to the maternal residence. The air quality report of the website included the hourly, daily and monthly air quality levels of each air pollutant. Information on exposure to air pollutants was collected monthly. The daily average was obtained and the maximum daily concentration was also averaged of $PM_{2.5}$, PM_{10}, and O_3 for each of the three pregnancy trimesters, i.e., first trimester (week 1 to 13), second trimester (week 14 to 26), and third trimester (week 27– delivery). The date of conception was estimated on the basis of the first day of the mother's last menstrual period.

2.3. Population

A case-control study was conducted in the Toxicology Lab of the Faculty of Chemistry of the UAEM in collaboration with the Gyneco-Obstetrics Hospital 221 (GOH 221) from the Instituto Mexicano del Seguro Social in the Toluca city, State of Mexico. The hospital has coverage of the rural, suburban and urban municipalities of the study area with a medium-low socioeconomic status. A total of 74 pregnant women and their premature newborns were recruited. The protocol was approved by the Institutional Research and Ethics Committee of GOH 221.

2.4. Selection of participants

A cohort of 74 pregnant women and their premature newborns was followed up, from which 44 were healthy women and 30 were diagnosed with preeclampsia giving written informed consent and blood samples at the time of diagnosis at hospital admission. The diagnosis of preeclampsia was made by a qualified Gynecologist-Obstetrician using the diagnostic criteria of the American College of Obstetrics and Gynecology (Roberts et al., 2013). Blood pressure (BP) was taken in the supine position of the left arm using an automatic digital sphygmomanometer, BP measurements were taken 4 h apart. Preeclampsia without severe features was defined when systolic blood pressure (SBP)/diastolic blood pressure (DBP) was 140/90 mmHg or higher in both (2 times with at least 4 h of difference after 20 weeks of gestation in a woman with a previously normal blood pressure); while preeclampsia with severe features was defined when the SBP/DBP was 160/110 or higher in both. The main clinical data of the study women (severity of maternal disease, maternal age and gestational age), anthropometric data (weight, height), and biochemical results were collected according to routine institutional guidelines. The clinical record and evolution of all premature newborns ≤36 weeks of gestational age included in the study were reviewed to collect the variables that were captured on a sheet designed specifically for said study (birth weight, gestational age, sex, neonatal morbidity during hospital stay: presence or absence of pathology (IUGR, RDS, IVH, NEC, BPD, NEC and ROP).

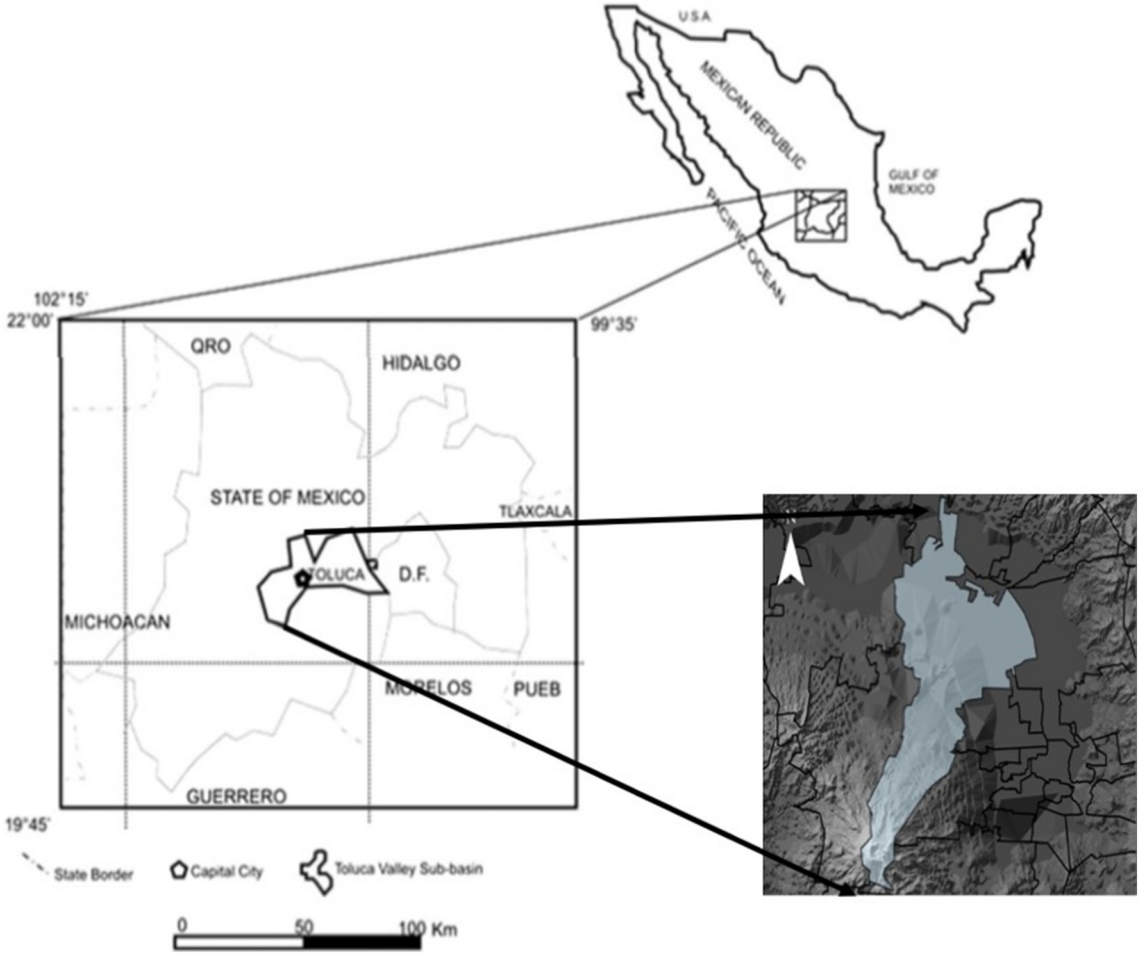

Fig. 1. MZTV is located between parallels 18° 59′ 07″ and 19° 34′ 47″ of north latitude, 99° 38′ 22″ and 99° 56′ 13″ of west longitude with respect to the prime meridian. The average height is 2600 with a range from 2560 to 2740 m above sea level. It is considered one of the most important metropolises in central Mexico with a highly polluted industry zone that presents a great variety of suspended particulate matter.

Intrauterine growth restriction (IUGR) is defined as fetal growth less than the normal growth potential. Refers to weight below the 10 percentile for gestational age, corrected for parity and gender, as per the population growth charts (Murki, 2014). Bronchopulmonary dysplasia (BPD) was defined as the need for supplemental oxygen at 36 weeks postmenstrual age, according to the new classification (Higgins et al., 2018). The need for ophthalmoscopic examination was performed in all newborns <32 weeks and in all those who needed O_2 therapy for early diagnosis of retinopathy of prematurity (ROP). Respiratory distress syndrome (RDS) was diagnosed on the presence of typical clinical and radiological signs: tachypnea, grunting and cyanosis with several hours of birth required mechanical ventilation and typical radiographic findings on the chest X-ray. The diagnosis was established from the clinical symptoms and needed for oxygen treatment (Negi et al., 2015). Intraventricular hemorrhage (IVH): bleeding in the subependymal germinal matrix. Extension is recorded by means of brain ultrasound scanning between the first 48 h and the first week of life, classified according to Volpe (Volpe, 1989) and Necrotizing enterocolitis (NEC): intestinal disease secondary to a complex interaction between immaturity, mucosal lesion secondary to various factors and a poor response of the patient to the lesion. Reported according to the modified Bell classification, there are 3 stages with subtypes A and B (Gregory et al., 2011). A serial identification code was provided to each woman and newborn for biological samples and clinical information, the mothers of newborns signed an informed consent prior to the interruption of the pregnancy. None of the procedures caused any additional stress or risk to mothers or newborns.

2.5. Study design

Pregnant women were divided into 2 groups. The study group: pregnant women with a diagnosed of preeclampsia, this group was also classified according to the severity of preeclampsia and the control group: healthy pregnant women. For newborns, the study group consisted of 30 premature newborns of women with preeclampsia. The control group was composed of 44 premature newborns of healthy women.

2.6. Exclusion criteria

Maternal history of type 1 or type 2 diabetes mellitus, gestational diabetes, previous hypertension, chronic heart, lung or kidney disease, infections, anemia, vaginal bleeding. Smoking during pregnancy (maternal active and passive smoking status), exposure to environmental tobacco smoke prior to the beginning of pregnancy, alcohol consumption during pregnancy and use of firewood or charcoal to cook food. Newborns at term, with congenital anomalies or with umbilical cord abnormalities, the presence of meconium in the amniotic fluid and fetal distress.

2.7. Collection and storage of samples

3 mL of blood sample (in heparinized and non-heparinized tubes) were obtained from women diagnosed with preeclampsia and healthy women's arm veins under aseptic conditions and sterile vacutainer upon admission to the unit. A 2 mL-blood sample was also obtained immediately after cutting the umbilical cord of newborns; to ensure a good filling of the vessels, a

clamp was placed 3 cm from the newborn's skin and a second clamp 10–20 cm away from the first clamp, the umbilical cord was cut and tied off; eventually the corresponding sample was obtained at the excess end of the umbilical cord. Blood samples were centrifuged at 5000 rpm for 10 min, the plasma/serum was separated and stored at 4 °C and subsequently frozen at −80 °C until analysis in the laboratory. The placentas were collected within 10 min after delivery, three main regions (central region, middle placenta and peripheral region) were sampled and deposited in a 4 °C heat-cooling vessel to transfer them to the research Toxicology Lab. of the Faculty of Chemistry of the UAEM. The samples were stored at −80 °C for later analysis. Homogenates at 10 % with 10 mM phosphate buffer at pH 7.4 were prepared for sample processing; they were centrifuged at 2000 rpm for 5 min and 3 mL of the supernatant was extracted for analysis.

2.8. Determination of the biomarkers of the oxidant and antioxidant state

For the biochemical analysis, the samples remained encoded until the analysis was completed. Enzymatic levels and oxidative markers (lipoperoxides, hydroperoxides, protein carbonyl) were measured from maternal plasma and umbilical cord, as well as placental tissue using an Epoch All-In-One Microplate reader (BioTek Instruments, Winooski, VT, USA), Gen5 Software version 2.09. The samples were assayed in triplicate for statistical purposes.

2.9. Determination of hydroperoxides content

The determination was made following the method of (Jiang et al., 1992). 100 μL of sample [previously deproteinized with 10 % trichloroacetic acid (Sigma-Aldrich)] was taken and 900 μL of the reaction mixture [0.25 mM $FeSO_4$ (Sigma-Aldrich), 25 mM H_2SO_4 (Sigma-Aldrich) were added, 0.1 mM xylenol orange (Sigma-Aldrich) and 4 mM butylated hydroxytoluene (Sigma-Aldrich) in 90 % (v/v) methanol (Sigma-Aldrich)]. The mixture was incubated for 60 min at room temperature and the absorbance at 560 nm was determined against a blank one containing only the reaction mixture. The results were extrapolated on a standard curve and expressed in nM HPC (Sigma-Aldrich)/mg protein.

2.10. Determination of the degree of lipoperoxidation

The determination of the degree of lipid peroxidation was carried out following (Buege and Aust, 1978) method. For 100 μL of the no-centrifuged sample, 150 mM Tris-HCl buffer solution pH 7.4 (Sigma-Aldrich) were added to complete 1 mL. The sample was incubated at 37 °C for 30 min, then 2 mL of TCA-TBA [thiobarbituric acid (Sigma-Aldrich) at 0.375 % in trichloroacetic acid (Sigma-Aldrich) at 15 %] was added, then a thermal shock (with the help of a water bath) in boiling water for 45 min. After this time, it was centrifuged at 3000 rpm for 10 min and the absorbance at 535 nm was determined. The results were expressed in mM of MDA/mg of protein, using the EMC of 1.56×10^5 M/cm.

2.11. Determination of protein carbonyl

The determination was made following the methodology of (Levine et al., 1994) modified by (Parvez and Raisuddin, 2005) and (Burcham, 2007). 150 μL of 10 mM DNPH (Sigma-Aldrich) in 2 M HCl (Sigma-Aldrich) were added to 100 μL of the supernatant. It was incubated for 1 h in the dark at room temperature. After incubation, 500 μL of 20 % trichloroacetic acid (Sigma-Aldrich) was added and let rest for 15 min at 4 °C. The precipitate was centrifuged at 11,000 rpm for 5 min. The button was washed several times with ethanol (Sigma-Aldrich) -ethyl acetate (Sigma-Aldrich) 1: 1 and subsequently dissolved in 1 mL of a 6 M solution of guanidine (Sigma-Aldrich) pH 2.3 and incubated at 37 °C for 30 min. The absorbance was determined at 366 nm. The results were expressed in μM of reactive carbonyls (C = O)/mg of protein, using the EMC of 21,000 M/cm.

2.12. Determination of superoxide dismutase activity

Superoxide dismutase activity was determined by developing (Misra and Fridovich, 1972). 40 μL of the homogenate were placed in a quartz cell and 260 μL of 50 mM carbonate buffer solution (50 mM sodium carbonate (Sigma-Aldrich) and 0.1 mM EDTA (Vetec)) was added at pH 10.2. Afterwards, 200 μL of 30 mM adrenaline (Bayer) were added and the absorbance at 480 nm was determined at 30 s and 5 min. The results were expressed as IU/mg protein.

2.13. Determination of catalase activity

It was performed following the method of (Radi et al., 1991). 20 μL of the supernatant were placed in a quartz cell, 1 mL of isolation buffer [sucrose (Vetec) 0.3 M, 1 mM EDTA (Vetec), 5 mM HEPES (Sigma-Aldrich) and KH_2PO_4 (Vetec) were added 5 mM] and 0.2 mL of a solution of H_2O_2 (Vetec) 20 mM. Subsequently, absorbance readings were made at 240 nm, at 0 and 60 s. The results were obtained by substituting the absorbance value obtained for each of the times in the formula: concentration of CAT = [(A0-A60)/CEM], where the CEM of H_2O_2 is 0.043 mM/cm, and they were expressed as μM H_2O_2/mg protein.

2.14. Determination of glutathione peroxidase

It was determined by the method of (Gunzler and Flohe-Clairborne, 1985) modified by (Stephensen, 2000). 100 μL of the supernatant were placed in a quartz cell and 10 μL of GR [2 U GR, (Sigma-Aldrich)] were added, in addition to 290 μL of the 50 mM reaction buffer [K_2HPO_4 (Vetec), KH_2PO_4 (Vetec) 50 mM pH 7.0, GSH (Sigma-Aldrich) 3.5 mM, 1 mM sodium azide (Sigma-Aldrich), NADPH (Sigma-Aldrich) 0.12 mM)] and 100 μL H2O2 (Vetec) 0.8 mM. Subsequently, the absorbance at 340 nm was determined at 0 and 60 s. The results were obtained using the following equation: GPx concentration = [(A0-A60)/CEM], where the NADPH EMC is 6.2 mM/cm. The results were expressed as mM NADPH/mg protein.

2.15. Statistical analysis

Data description was presented as means ± SD to describe distribution of continuous variable and categorical data as percentages. The normality of distributions was evaluated with the One-sample Kolmogorov–Smirnov test. For comparison of the groups, independent bivariate *t*-test was used for values with normal distribution. The non-parametric Mann–Whitney *U* test and the Wilcoxon signed rank test were used to determine the differences between the variables not showing normal distribution. Odds ratio (OR) with corresponding 95 % confidence intervals (CI) were calculated to explore the associations between neonatal diseases and preeclampsia. In oxidative stress biomarkers in neonatal diseases associated with preeclampsia, multiple comparisons between groups were performed by one-way analysis of variance and the significant differences of each group were compared using the Tukey-Kramer test and their association with preeclampsia was determined with Pearson's correlation test. Values of $P < 0.05$ were taken as significant. Data were analyzed by statistical SPSS v10 software (SPSS, Chicago IL, USA). The Principal component analysis (PCA) was performed using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Australia).

3. Results

3.1. Biochemical characteristics and parameters

Tables 1 show the characteristics of pregnant women and their newborns. According to the anthropometric results a higher body weight was also reported in pregnant women who developed preeclampsia ($p < 0.01$). Meanwhile, there were no statistically significant differences in the maternal age, gestational age and birth weight of the newborns compared

Table 1
Characteristics and biochemical parameters of the groups.

Variable	Healthy women $n = 44$	PE $n = 30$	*P value
Demographic characteristics			
Maternal age (years)	27.2 ± 8.2	31 ± 7.1*	NS
Weight (kg)	71.4 ± 11.1	58.1 ± 6.4*	< 0.01
Gestational Age (weeks)	32.5 ± 2.4	33.4 ± 2.2	NS
Birth weight (grams)	1876 ± 606.8	1876.4 ± 583.6	NS
Pregnancy number	2.2 ± 1	1.8 ± 0.9	NS
Blood pressure			
Systolic pressure (mm Hg)	112.5 ± 10.2	156.9 ± 13.6*	< 0.001
Diastolic pressure (mm Hg)	69 ± 7.7	105.7 ± 9*	< 0.001
Biochemical results			
Platelets (10^3/μL)	300 ± 96.2	175 ± 79.3*	< 0.001
Creatinine (mg/dL)	0.5 ± 0.06	0.9 ± 0.8	NS
AST (U/L)	18.1 ± 8.5	146.4 ± 66.6*	NS
ALT (U/L)	12 ± 7.5	126 ± 54.1*	< 0.05
DHL (U/L)	132.6 ± 57.6	474.1 ± 145.7*	< 0.05
	n (%)	n (%)	Total n (%)
Education level			
College and above	5 (11.3)	3 (10)	8 (10.8)
Junior college/Bachelor	9 (20.4)	6 (20)	15 (20.2)
High school	17 (38.6)	10 (33.3)	27 (36.4)
Primary school and below	13 (29.5)	11 (36.6)	23 (31)
Socioeconomic status			
High	1 (2.2)	2 (6.6)	3 (4)
Medium	22 (50)	12 (40)	34 (45.9)
Low	21 (47.7)	16 (53.3)	37 (50)

Note: Data are presented as mean ± SD. 95 % confidence interval for the mean. n (%) for categorical variable. Significant *$p < 0.001$, $p < 0.01$ and $p < 0.05$. NS: not significant. PE = Women with preeclampsia.

to the control group. Both systolic and diastolic pressure were significantly higher in the group of women with preeclampsia ($p < 0.001$) (Table 1).

When comparing serum and urinary biochemical markers in the study groups (Table 1) the platelet levels decreased significantly in pregnant women with preeclampsia and women with severe features preeclampsia ($p < 0.001$). Serum levels of ALT and DHL were significantly higher in women with preeclamptic women compared to healthy pregnant women group ($p < 0.05$); however, serum creatinine levels and AST were similar between groups.

3.2. Exposure to air pollutants

The concentration of exposed $PM_{2.5}$, PM_{10} and O_3 in the first, second and third trimesters of pregnancy was shown in Table 2. The median and maximum concentrations of exposed $PM_{2.5}$, PM_{10} and O_3 in preeclampsia group were higher than those in control group in the first two trimesters ($p < 0.05$). There was no significant difference between the two groups in the concentration of $PM_{2.5}$ and PM_{10} exposed in the third trimester ($p < 0.05$). While for ozone there was a significant difference in the last trimester in the maximum exposure.

Table 3
Analysis of the concentration of exposure to ambient air pollutants during the study period.

Pollutant	$PM_{2.5}$ (μg/m^3)	PM_{10} (μg/m^3)	O_3 (ppm)
Minimum concentration	16.7	36.2	0.02
Maximum concentration	227.1	389.8	0.15
Q1	34.2	54.8	0.05
Q2	44.3	74.3	0.07
Q3	61	115.4	0.09
IQR	27.1	62.3	0.05

Results obtained from the analysis using exposure-specific quartiles showed that during the study period, Table 3.

The concentration of exposed ambient air pollutants ($PM_{2.5}$, PM_{10} and O_3) in the study period was stratified into three groups according to quartile (Q1, Q2, Q3).

Fig. 2 a) and b) show the areas with the highest concentration of PM_{10} and PM $_{2.5}$ found to the northeast of the study area - (SC and SM) of the ZMVT. This is justified by the use of land in these areas, to the north (SC) livestock use and to the east (SM) is an Industrial area. Likewise, Toluca is an area of great vehicular influx, connecting the Mexican capital with the capital of the Mexican Republic. c) shows the result of the interpolation of the values obtained by O_3 in the ZMVT indicating the pollution levels. The most affected area is the one adjacent to the MT station, being an area of housing-residential, commercial, tourist and recreational affluence.

3.3. Neonatal diseases associated with preeclampsia

Newborns born to preeclamptic women were included as cases and newborns born to normotensive women as control group. Neonatal diseases are highly associated with the development of preeclampsia, mainly intrauterine growth restriction (IUGR) and necrotizing enterocolitis (NEC) (Table 4). Statistical analysis indicated that newborns of women with preeclampsia were more likely to suffer from IUGR, NEC and BPD. There was no significant difference in the presence of RDS, IVH and ROP in the newborns of preeclamptic women.

3.4. Markers of oxidative stress in the study groups

Table 5 shows the levels of oxidative damage markers and total antioxidant activity in the different studied groups. Levels of the extent of protein oxidation expressed by protein carbonyl, the product of lipid peroxidation –

Table 2
Concentration of exposure to air pollutants in the first to third trimester of pregnancy.

Variable	Healthy women (max c) $n = 44$	PE (max c) $n = 30$	*P value	Healthy women (median c) n = 44	PE (median c) n = 30	*P value
Pollutants						
$PM_{2.5}$ (μg/m^3)						
Trimester 1	66 ± 16.6	86.7 ± 30.7	<0.05	41 ± 7.3	49.6 ± 13.9	<0.05
Trimester 2	66.1 ± 22.2	91.4 ± 45.6	<0.05	44.3 ± 15.4	51.3 ± 17.5	<0.01
Trimester 3	69.7 ± 11.8	75.8 ± 23.8	NS	48.4 ± 13.6	46.3 ± 13.8	NS
PM_{10} (μg/m^3)						
Trimester 1	119.4 ± 32	155.1 ± 48	<0.05	69.3 ± 15.3	88.8 ± 32.3	<0.05
Trimester 2	111.1 ± 40.2	160.3 ± 76.9	<0.05	74.6 ± 34.6	91.7 ± 39.4	<0.05
Trimester 3	135.5 ± 34.9	130.9 ± 35	NS	85.1 ± 23.3	84.7 ± 31.8	NS
O_3 (ppm)						
Trimester 1	0.101 ± 0.006	0.108 ± 0.008	<0.05	0.072 ± 0.007	0.078 ± 0.007	<0.01
Trimester 2	0.101 ± 0.008	0.109 ± 0.015	<0.05	0.072 ± 0.006	0.075 ± 0.006	<0.05
Trimester 3	0.104 ± 0.004	0.111 ± 0.013	<0.05	0.075 ± 0.008	0.074 ± 0.007	NS

Note: The maximum concentration as median (interquartile ranges) of exposure to air pollutants were presented. Data are presented as mean ± SD. 95 % confidence interval for the mean. Significant *$p < 0.05$. NS: not significant. Max c. = maximum concentration, median c = median concentration, PE = Women with preeclampsia. Trimester 1 = the first trimester of pregnancy, Trimester 2 = the second trimester of pregnancy, Trimester 3 = the third trimester of pregnancy, ppm = units of measure are in parts per million.

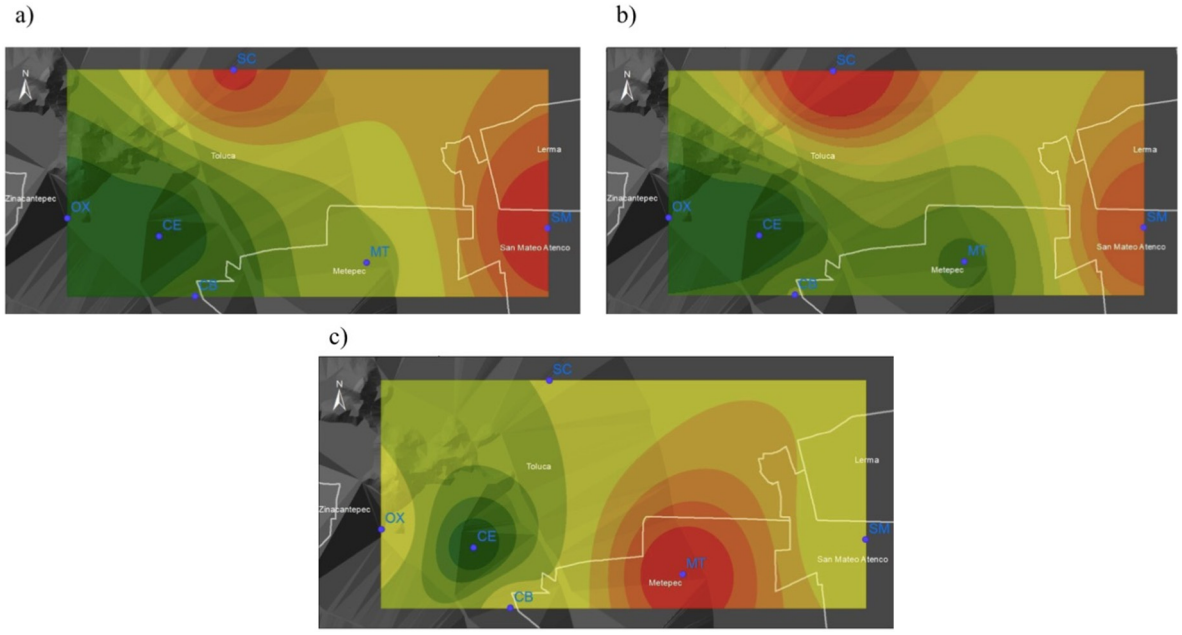

Fig. 2. Dispersion analysis of ambient air pollutants during the study period. The analysis and interpretation of the parameters of the ambient air pollutants, their behavior and their relationship with the wind reported by the RAMA-ZMVT are shown. These maps were made based on the measurements made by the RAMA-ZMVT in the years 2017–2018 through IDW interpolation.

Malondialdehyde (MDA), and hydroperoxides were significantly increased in placental tissue and serum from women with preeclampsia compared to normal pregnancies. Meanwhile, the levels of these markers of oxidative damage increased significantly in newborns of preeclamptic pregnant women compared to control group, protein carbonyl ($p < 0.01$), MDA ($p < 0.05$) and hydroperoxides ($p < 0.05$). Whereas, the activity of catalase (CAT) and superoxide dismutase (SOD) decreased significantly in umbilical cord blood ($p < 0.01$) and ($p < 0.05$) respectively. In placenta and serum from women who developed preeclampsia, CAT ($p < 0.01$) and SOD ($p < 0.05$) levels decreased significantly. Glutathione peroxidase (GPx) activity decreased in the preeclampsia group in placental tissue ($p < 0.05$) and serum ($p < 0.01$); meanwhile, the enzyme activity was significantly increased in newborns of women with preeclampsia ($p < 0.05$) compared with the control group.

3.5. Oxidative stress biomarkers in neonatal diseases associated with preeclampsia

Oxidative stress markers in IUGR and NEC as diseases associated with preeclampsia are shown in Figs. 3 and 4. In newborns of pregnant women with preeclampsia who developed IUGR, increased levels of MDA ($p < 0.05$), protein carbonyl ($p < 0.001$) and hydroperoxides ($p < 0.05$)

Table 4
Neonatal diseases associated with preeclampsia.

Disease	Newborns of healthy women Control $n = 44$ (%)	Newborns – PE n = 30 (%)	* *P* value	OR (95 % CI)
IUGR	10 (22.7)	20 (66.7)	<0.001	6.8 (2.4–19.1)*
RDS	20 (45.4)	10 (33.3)	NS	0.6 (0.2–1.5)
NEC	9 (20.4)	16 (53.3)	<0.001	4.4 (1.5–12.3)*
IVH	12 (27.3)	10 (33.3)	NS	1.3 (0.4–3.6)
BPD	4 (9.1)	8 (26.7)	<0.001	3.6 (1.5–13.4)*
ROP	6 (13.6)	6 (20)	NS	1.5 (0.4–5.4)

Note: Data are presented as n (%) for categorical variable. 95 % confidence interval for the mean. PE = Women with preeclampsia, IUGR = Intrauterine growth restriction, RDS = Respiratory distress syndrome, NEC = Necrotizing Enterocolitis, IVH = Intraventricular hemorrhage, BPD = Bronchopulmonary dysplasia, ROP = Retinopathy of prematurity. Significant *$p < 0.001$. NS: not significant.

Table 5
Comparison of oxidative stress markers in women with preeclampsia (maternal serum/placenta) and newborn infants.

	Biomarkers placental tissue oxidative stress		Biomarkers serum oxidative stress		Biomarkers umbilical cord	
	Control group $n = 44$	PE $n = 30$	Control group n = 44	PE n = 30	Control group n = 44	Newborns – PE n = 30
Protein carbonyl (μM reactive carbonyls/mg protein)	1.4 ± 0.3	2.6 ± 0.2[a]	0.7 ± 0.04	1.09 ± 0.1[c]	0.7 ± 0.06	1.1 ± 0.1[b]
Lipid peroxidation (mM MDA/mg protein)	58.09 ± 2.2	76.9 ± 7.1[b]	45.7 ± 2.3	54.3 ± 2.4[b]	33.4 ± 3.8	50.5 ± 3.3[a]
Hydroperoxide content (nM CHP/mg protein)	4.2 ± 0.6	7.7 ± 0.8[c]	4.8 ± 0.2	5.7 ± 0.2[c]	3.7 ± 0.3	5.4 ± 0.6[a]
CAT activity (μM H_2O_2/mg protein)	2324.2 ± 882.3	1521.7 ± 276.6[b]	1042.1 ± 189.3	768.9 ± 196.5[a]	1178.8 ± 201.7	651.6 ± 130.8[b]
GPx activity (μM NADPH/mg protein)	0.87 ± 0.2	0.4 ± 0.09[a]	1.1 ± 0.3	0.6 ± 0.1[b]	1.6 ± 0.4	2.3 ± 0.4[a]
SOD activity (IU SOD/mg protein)	7.5 ± 1.03	4.9 ± 1.3[a]	4.01 ± 0.89	2.7 ± 0.1[a]	4.6 ± 0.5	3.4 ± 0.6[a]

Note: Data are presented as mean ± SD. 95 % confidence interval for the mean. n (%) for categorical variable. Significant *$p < 0.001$, $p < 0.01$ and $p < 0.05$. NS: not significant. PE = Women with preeclampsia. Significant <0.05 (a), $p < 0.01$ (b), $p < 0.001$(c).

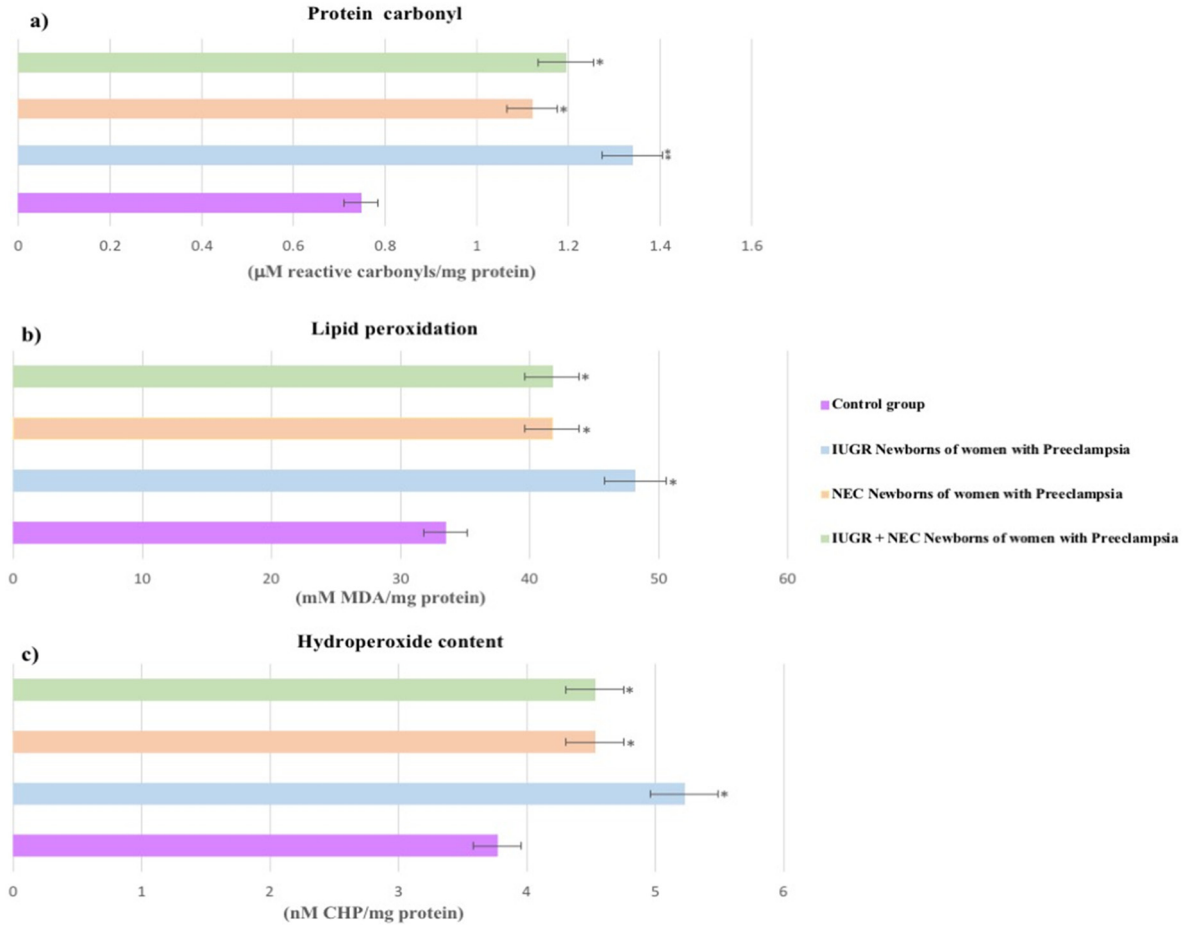

Fig. 3. Oxidative stress biomarkers in neonatal diseases. Concentrations of oxidative damage markers: protein carbonyl, hydroperoxides and MDA a) - c) in umbilical cord serum in preterm infants who presented diseases related to preeclampsia (IUGR, NEC and IUGR + NEC). Data are presented as mean ± SD. Indicates significant change compared to control group (*$p < 0.05$, **$p < 0.001$).

were observed compared to controls, while levels SOD ($p < 0.05$) and CAT ($p < 0.05$) decreased significantly. Levels of MDA ($p < 0.05$), protein carbonyl ($p < 0.05$) and hydroperoxides ($p < 0.05$) in the umbilical cord blood of newborns of preeclamptic women were significantly increased who developed NEC and the association of both diseases (IUGR + NEC), while the activity of CAT ($p < 0.05$) and SOD ($p < 0.05$) decreased in these diseases with respect to control group. Statistically higher significant difference in the levels of GPx in umbilical cord serum were found in newborns with preeclampsia-related diseases (IUGR ($p < 0.001$), NEC ($p < 0.05$) and IUGR + NEC ($p < 0.05$) compared with the control group.

3.6. Correlation of oxidative stress biomarkers and neonatal diseases associated with preeclampsia

Pearson's correlation analysis was performed to determine the relationship between oxidative damage markers and antioxidant enzymes in neonatal diseases associated with preeclampsia. A significant positive association was observed in the levels of protein carbonyl ($r = 0.71$, $p < 0.05$), MDA ($r = 0.38$, $p < 0.05$), hydroperoxides ($r = 0.69$, $p < 0.05$) and GPx activity ($r = 0.32$, $p < 0.05$) with IUGR. An inverse correlation was identified between CAT activity with the risk of IUGR and NEC ($r = -0.61$, $p < 0.05$) and ($r = -0.43$, $p < 0.05$), respectively. There was no statistically significant correlation of protein carbonyl, MDA, hydroperoxides, GPx activity, and SOD when NEC was present. When IUGR and NEC were associated, a positive correlation was found with MDA levels ($r = 0.96$, $p < 0.05$) in umbilical cord blood, while a negative correlation was found with SOD activity ($r = -0.32$, $p < 0.05$). No statistically significant correlation was found between the association of IUGR and NEC with the levels of protein carbonyl, hydroperoxides and GPx activity.

3.7. Principal component analysis (PCA) and cluster analysis

Principal components analysis was carried out to identify the correlation of standardized biomarker levels and neonatal diseases associated with preeclampsia. The components were responsible for 56.1 % of the total variance. Cluster analysis using principal components grouped newborns of preeclamptic women into three study groups and one control group. The PCA loading plots (Fig. 5), showing the relationships between oxidative stress biomarkers in PC1 and PC2, we find a strong positive correlation between increased levels of MDA, hydroperoxides, protein carbonyl and GPx activity; in addition, to a negative association on SOD and CAT activity in the group of newborns who presented IUGR. While, in the NEC group, a negative correlation was observed in the enzymatic activity of CAT. When the presence of IUGR and NEC in newborns is related, a positive correlation was obtained in the levels of MDA and a negative correlation in the enzymatic activity of SOD.

4. Discussion

4.1. Air pollution exposure and preeclampsia

Air pollution exposure can affect both mother and the developing foetus. The etiopathogenesis of preeclampsia is considered multifactorial. Therefore, potential factors such as increased ambient air pollutants may account this condition (Sun et al., 2020). Our study found that the

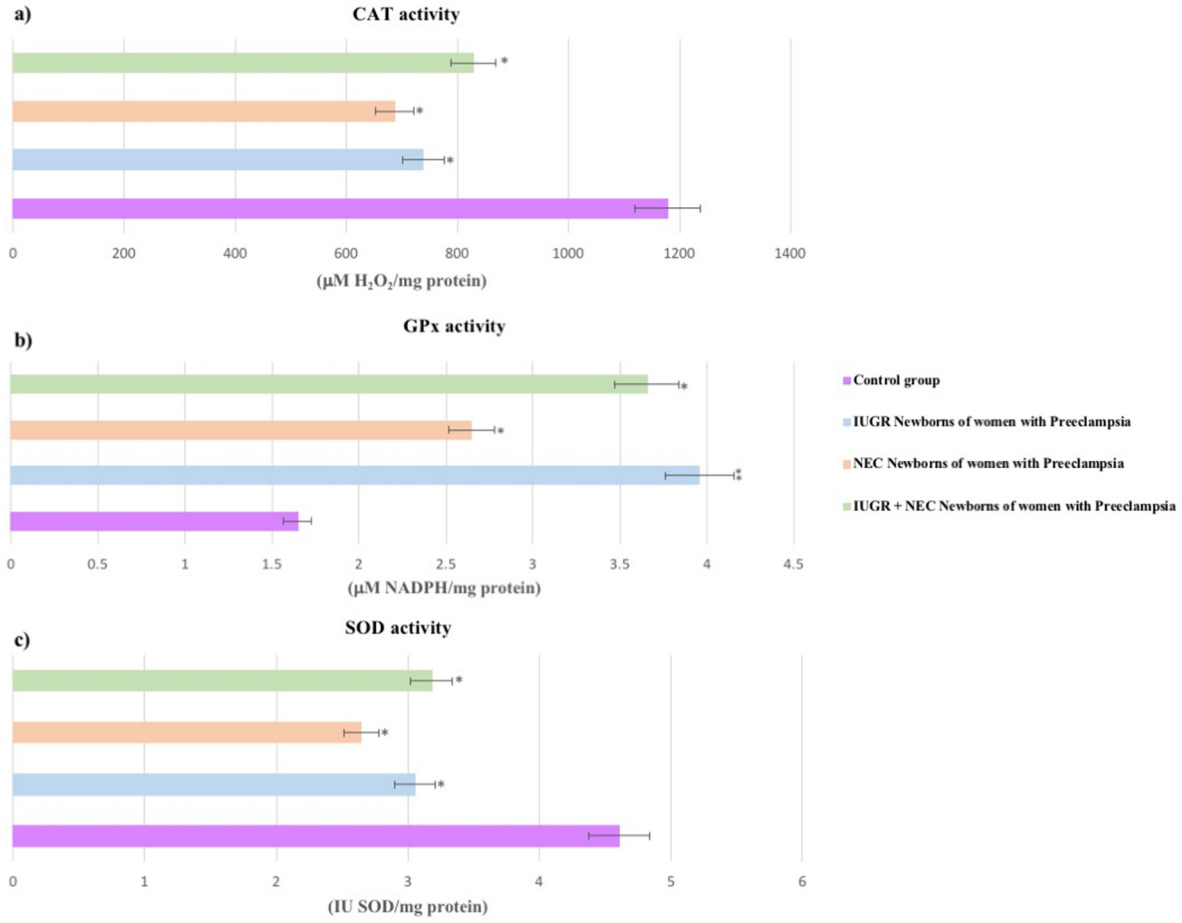

Fig. 4. Antioxidant enzyme activity. Concentration of antioxidants a) - c) in umbilical cord blood of preterm infants with neonatal diseases associated with preeclampsia. Data are presented as mean ± SD. * Indicates significant change compared to control group (*$p < 0.05$, **$p < 0.001$).

concentrations of exposed $PM_{2.5}$, PM_{10} and O_3 in preeclampsia patients were higher than those in women without preeclampsia in the first and second trimesters, the same reported by (Jia et al., 2020). (Mandakh et al., 2020) reported a risk for the development of preeclampsia associated with exposure to ambient air pollutants during entire pregnancy in a low-exposure area in southern Sweden, and further risk of pregnancies with small-for-gestational age complications. While in Barcelona, Spain (Dadvand et al., 2013) found positive associations for the presence of preeclampsia associated with exposure to fine particulate pollutants in the first and third trimesters of pregnancy. Subsequently, (Dadvand et al., 2014) observed an increased risk of preeclampsia associated with exposure to fine particulate pollutants during entire pregnancy. Recently (Dastoorpoor et al., 2021) observed that levels of environmental air pollutants showed direct and significant associations with preeclampsia in Ahvaz, Iran. In contrast, (Nobles et al., 2019) published that higher levels of environmental pollutants in the first trimester were associated with lower preeclampsia risk, while higher levels in the second trimester were associated with greater gestational hypertension risk, a study in Utah, USA. In New York, (Assibey-Mensah et al., 2020) reported that an increase in fine particle concentration was associated with an increased early-onset preeclampsia risk during the first trimester of pregnancy. However, (Savitz et al., 2015) did not find evidence of an association between exposure to $PM_{2.5}$ and NO_2 during the first and second trimesters of pregnancy and any risk of mild or severe preeclampsia and Rudra et al. showed no significant association between $PM_{2.5}$ exposure and preeclampsia in a prospective study (Rudra et al., 2011). In Rhode Island, (Choe et al., 2018) observed no risk of preeclampsia associated with $PM_{2.5}$ exposure during each trimester of pregnancy. Meanwhile, in our study the exposure level of O_3 in preeclampsia women was higher than that in control group in the third trimester. A study in the Florida and one more in Japan, reported a higher exposure to O_3 and its relationship with hypertensive disorders of pregnancy (Hu et al., 2017; Michikawa et al., 2015). Patients with preeclampsia had higher concentration of O_3 exposure during pregnancy, according to what was observed by (Jia et al., 2020). Mean concentration of $PM_{2.5}$ exposure over the entire pregnancy was 44.31 μg/m^3 between 2017 and 2018, concentrations similar to a study in China conducted by (Yuan et al., 2020). It is important to mention that the maximum concentrations reported for $PM_{2.5}$, PM_{10} and O_3 in the study period were higher than the EU reference values, European Union Air Quality Directive and WHO Air Quality Guidelines (Hoffmann et al., 2020).

The women in our study are population of medium-low socioeconomic status and education level. According to some studies, younger subjects, less educated, exposed to passive smoking, low to middle household income, overweight, without ventilation system at home or office, and do not possess private vehicles, are more susceptible to ambient air pollutants (Liang et al., 2019).

4.2. Oxidative stress in preeclampsia and air pollution exposure

Pregnant women are more susceptible to oxidative stress due to physiological changes and increased energy expenditure. Adverse pregnancy and birth outcomes have been associated with exposure to ambient air pollution and oxidative stress as a mechanism (Feng et al., 2016; Nagiah et al., 2015). There is evidence has suggested that elevated malondialdehyde levels are linked to exposure to ambient air pollution (Li et al., 2020). In Scania, Sweden (Mandakh et al., 2021) observed an association between prenatal exposure to ambient nitrogen oxides and the presence of preeclampsia through oxidative damage in the 1st trimester. In our study show that

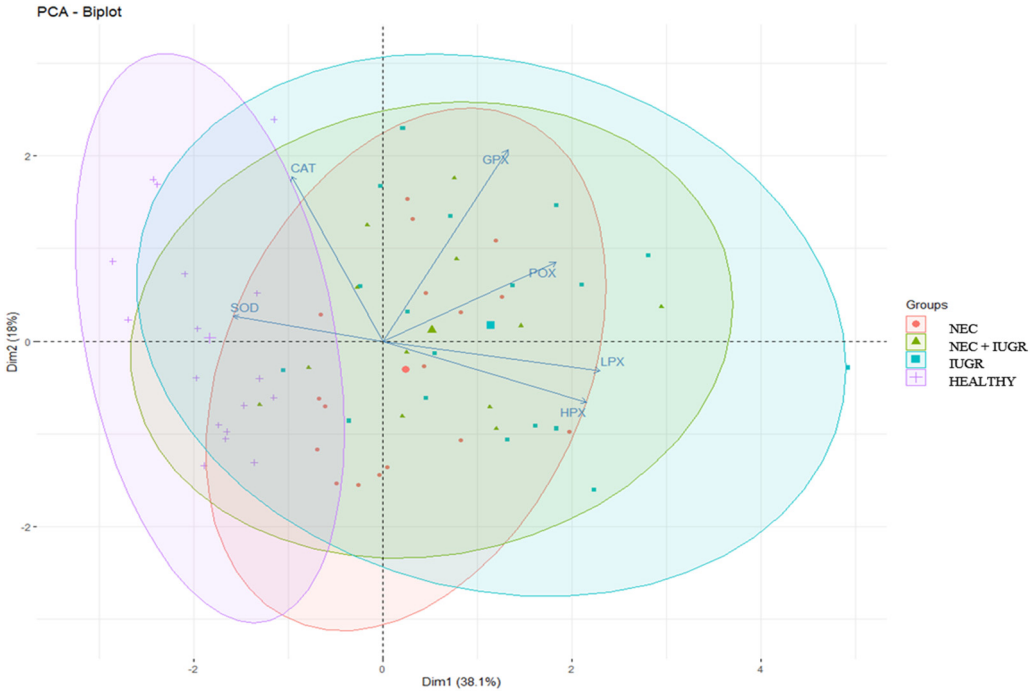

Fig. 5. Principal component analysis of neonatal diseases. Principal component analysis Biplot (PCA Biplot) combines the score plots and the loading plots showing the values of the linear combinations and the loads. Variable distribution plots assayed between the measured oxidative stress biomarkers. POX- protein carbonyl; LPX- lipid peroxidation (MDA); HPX- hydroperoxides. NEC-Necrotizing Enterocolitis (pink circle); IUGR-Intrauterine growth restriction (blue square); NEC + IUGR (green triangle); Healthy (purple cross). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

oxidative stress markers were significantly higher in women with preeclampsia and their newborns who were exposed to higher levels of ambient air pollutants compared to the control group, similar results to what was reported by (Grevendonk et al., 2016; Nagiah et al., 2015). While in the same study a significant elevation in the levels of the SOD2 enzyme is reported in the women from heavy industrial areas. We observed a decrease in SOD activity in women with preeclampsia and in their newborns, as well as in GPx and CAT activity. This indicates that exposure to air pollution during pregnancy does increase the susceptibility to oxidative stress and the development of adverse outcomes.

4.3. Oxidative stress and preeclampsia

Maternal and perinatal morbidity and mortality due to preeclampsia has been drastically reduced in developed countries, in contrast to what was reported in third world countries. The imbalance between the generation of reactive oxygen species (ROS) or reactive nitrogen species (RNS) and antioxidant capacity defines oxidative stress (Sinha and Dabla, 2015). When oxidative stress overcomes antioxidant defense in the placenta, free radicals released from the poorly perfused fetoplacental unit cause disruption of the placental endothelial function and oxidative damage that spreads to distal tissues, as seen in preeclampsia (Aouache et al., 2018; Hansson et al., 2015; Phaniendra et al., 2015). The main cause of oxidative stress in preeclampsia is hypoxia-reperfusion events, are the source of ROS and are associated with oxidative damage, inflammatory response and antioxidant defense depletion (Guerby et al., 2021; Sanchez-Aranguren et al., 2014; Schoots et al., 2018; Tenório et al., 2019). The uteroplacental hypoperfusion during preeclampsia increases oxidative stress in both the mother and the fetus. Increased reactive oxygen species can lead to irreversible cellular damage, necrosis, and apoptosis from lipid peroxidation, protein damage and DNA oxidation. This results in cell damage and potential tissue injury (Burton and Jauniaux, 2011; Hansson et al., 2015; Zha et al., 2017).

Oxidative stress generates the peroxidation of polyunsaturated fatty acids, which originates a huge amount of lipoperoxides, hydroperoxides and aldehydes, which cause cell dysfunction, apoptosis and inflammation (Halliwell, 2007). The syncytiotrophoblast (STB) has a low concentration of antioxidant defense and their plasma membranes have abundant unsaturated fatty acids. Therefore, STB is more vulnerable to ROS injury. Placenta-derived lipid peroxides damage low-density lipoproteins in the circulating blood, causing their peroxidation and subsequent systemic lipid peroxidation, leading to maternal vascular dysfunction (Chiarello et al., 2020; Dash, 2003; Lorentzen and Henriksen, 1998). MDA is a product and biomarker of lipid peroxidation found to be elevated in the plasma of preeclamptic women (Hubel et al., 1989). Our study found higher concentration of product of lipid peroxidation - MDA and hydroperoxides in the preeclampsia group compared to normotensive women. High levels of ROS and MDA in women with severe preeclampsia have been reported (Liu et al., 2020). While, D'Souza et al., demonstrates an increase in MDA levels in preeclamptic women in the first and second trimesters (D'Souza et al., 2016). A meta-analysis concludes that lipid peroxidation is an important factor in the pathogenesis of preeclampsia, since a higher level of MDA was observed in preeclampsia women (Taravati and Tohidi, 2018). In newborns of women with preeclampsia we found elevated levels of MDA and hydroperoxides in the umbilical cord blood when compared to newborns of healthy women. Bharadwaj et al., Reported that of lipid peroxidation, malondialdehyde levels and protein carbonyl levels were significantly higher in the cord blood of neonates born to preeclamptic women (S. Bharadwaj et al., 2018a).

Lipid oxidation products lead to the oxidation of different amino acid residues of proteins and oxidative cleavage of proteins, generating protein carbonyl (useful and sensitive biomarker for oxidative stress-induced protein damage) (Chiarello et al., 2020; Phaniendra et al., 2015; Taravati and Tohidi, 2018). We found that protein carbonyl levels were higher in women who developed preeclampsia compared to control group. In addition, we found higher concentration of protein carbonyl in the umbilical cord blood of preeclamptic women compared to controls. Significant elevations of protein carbonyl levels in cord blood and preeclamptic women have been reported (S. K. Bharadwaj et al., 2018b; Negi et al., 2014; Taravati and Tohidi, 2018). Furthermore, a significant correlation was

reported between protein carbonyl levels in women with preeclampsia and cord blood, and consequently an adverse early neonatal outcome (S. Bharadwaj et al., 2018a).

Antioxidant enzymes (SOD, CAT and GPx) constitute the first line of defense against ROS (Birben et al., 2012). The hypothesis that oxidative defenses could increase at the beginning PE pregnancy has been raised (Taravati and Tohidi, 2018). However, not enough to counter oxidative damage in preeclampsia and neonatal outcome. Some studies have found significantly lower total antioxidant capacity in preeclamptic women (S. K. Bharadwaj et al., 2018b), whereas others studies report higher total antioxidant capacities (Shaarawy et al., 1998). Antioxidant defense probably is reduced in preeclampsia by due to a diminution activity of the antioxidant enzymes (Chiarello et al., 2020). We observed a low antioxidant enzymes CAT, SOD and GPx concentrations in the maternal circulation and in the placenta, while GPx activity was higher in umbilical cord blood compared to CAT and SOD activities in fetal circulation, which was lower. Publications report higher SOD activity in women with preeclampsia (Nikolic et al., 2016; Roy et al., 2015), whereas others found significantly lower activity (Negi et al., 2012; Pimentel et al., 2013). A meta-analysis concludes that SOD activity is lower in preeclamptic women (Taravati and Tohidi, 2018) and Cord plasma activity of superoxide dismutase was significantly lower in preterm infants (Norishadkam et al., 2017). Negi et al., observed a significant rise in the levels of carbonylated protein along with decreased levels of catalase in the umbilical cord blood of pregnancies with preeclampsia and eclampsia (Negi et al., 2014). Several studies show decreased CAT and SOD activity, and increased lipid peroxidation in the blood plasma from women with preeclampsia (Chiarello et al., 2020; García, 2016; Kumar and Das, n.d.). However, an increase in CAT and GPx activities was observed in preeclamptic women (Taravati and Tohidi, 2018). A few studies were found significantly lower GPx activity in women with preeclamptic (Chamy et al., 2006). Taravati and Tohidi reported a significant increase in GPx activity in preeclamptic women compared to normal pregnant women (Taravati and Tohidi, 2018). According to the above, the increase or decrease in the levels of antioxidant enzymes is probably determined by the trimester of gestation evaluated and the response to oxidative stress as a compensatory response to it, the state of adaptation as part of the metabolic response and, mainly the degree of biochemical alteration related to clinical severity. Increase in GPx levels in the fetal circulation found in our study could be explained by the fact that GPx is directly involved in the elimination of ROS to inhibit lipid peroxidation especially in the membrane phospholipids. The elevated levels may be an adaptive response to high levels of oxidative stress in later stages of preeclampsia (D'Souza et al., 2016). Higher significant activity of glutathione peroxidase and catalase reflect the persistence of oxidative stress. Increased glutathione peroxidase activity may probably serve as a compensatory mechanism to prevent further damage by reactive radicals (Knapen et al., 1999; Taravati and Tohidi, 2018).

4.4. Perinatal outcomes and preeclampsia

The perinatal outcomes of women who develop preeclampsia are high rates of perinatal mortality, IUGR and increased neonatal morbidity due to premature delivery. Likewise, NEC is reported with a higher incidence in newborns with IUGR (de Souza Rugolo et al., 2011). Our study reports that preeclampsia is associated with the risk of developing neonatal diseases such as IUGR, NEC and BPD in premature newborns. Yang et al., reports that maternal hypertension was associated with an increased risk: 1.86 times more development of neonatal NEC, and intrauterine growth restriction increases 3.59 times the development of NEC (Yang et al., 2018). On the other hand, the prematurity and IUGR were more among preeclamptic group a case control study in preeclamptic women (S. Bharadwaj et al., 2018a). No studies were found to determine the association between preeclampsia and BPD, however, they have been related to the presence of oxidative stress as a pathophysiological factor (Perrone et al., 2012).

Newborns, especially if preterm, are particularly prone to the action of free radicals due to, functional immaturity of organs, increase of tissue mass with aerobic metabolism and relative deficiency of antioxidant systems (Giuffrè et al., 2015; Mutinati et al., 2014). When we compared the presence of neonatal disease in preterm newborns with oxidative stress markers and antioxidant status, we found that when IUGR and NEC developed, levels of MDA, protein carbonyl, hydroperoxides, and GPx activity were elevated in umbilical cord blood. We also observed a significant reduction in CAT and SOD activity. Most of the studies showed a relationship between increased levels of oxidative stress biomarkers and/or decreased levels of antioxidants in cord blood and higher risk of clinical outcomes (de Almeida et al., 2021). Also observed that the imbalance between oxidant and antioxidant factors seems to play an important role in the onset of the main pathologies of the preterm infant, such as BPD and NEC (Falsaperla et al., 2020). A review by Casavant et al., showed that premature newborns had lower levels of catalase and to increased rates of NEC (Casavant et al., 2019).

4.5. Oxidative stress and perinatal outcomes

Our study established a positive correlation between the development of IUGR and the levels of protein carbonyl, MDA, hydroperoxides and GPx activity. An inverse correlation was identified between CAT activity with the risk of IUGR and NEC. When IUGR and NEC were associated, a positive correlation was found with MDA levels in umbilical cord blood, while a negative correlation was found with SOD activity. There is a clear association between OS markers and the risk of developing free radical-related diseases in preterm newborns (Perrone et al., 2010). Several studies showed a greater association with increased oxidative stress (advanced oxidation protein products and MDA) and/or reduced antioxidant levels and RCIU (Bandyopadhyay et al., 2017; de Almeida et al., 2021; Perrone et al., 2016; Silva et al., 2019). While, Ghany et al., described a significant relationship between decreased catalase levels at birth and the risk of ECN (Abdel Ghany et al., 2016). Early neonatal outcomes such as IUGR had significant correlation with protein carbonyl levels among cases in preeclamptic women (S. Bharadwaj et al., 2018a).

We conclude that OS has been identified in the pathogenesis of preeclampsia and neonatal disease. There is increased oxidative damage in both the maternal and fetal circulation in women who develop preeclampsia exposed to air pollution during pregnancy. Therefore, these pregnancies complicated by preeclampsia have a greater adverse outcome as neonatal disease in the preterm infant. It is important to early identify the critical exposure windows throughout gestation and to the newborns at risk of diseases associated with oxidative stress early and implement preventive measures before and during pregnancy, and the adoption of appropriate policies to diminish ambient air pollution emissions and to raise awareness of pregnant women. In addition, we propose that a research is needed to link pregnancy outcome data with spatially and temporally resolved ambient air pollution data.

CRediT authorship contribution statement

Sindy San Juan-Reyes and Nely San Juan-Reyes performed all the exposure experiments.

Leobardo Manuel Gómez-Oliván and Sindy San Juan-Reyes were involved in the conception.

Leobardo Manuel Gómez-Oliván, Sindy San Juan-Reyes and Nely San Juan-Reyes were involved in the design and interpretation of the data and the writing of the manuscript with input from Hariz Islas-Flores, Octavio Dublán-García, José Manuel Orozco-Hernández, Itzayana Pérez-Álvarez, & Alejandro Mejía-García.

Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Abdel Ghany, E.A.G., Alsharany, W., Ali, A.A., Youness, E.R., Hussein, J.S., 2016. Anti-oxidant profiles and markers of oxidative stress in preterm neonates. Paediatr. Int. Child Health 36, 134–140. https://doi.org/10.1179/2046905515Y.0000000017.

Aouache, R., Biquard, L., Vaiman, D., Miralles, F., 2018. Oxidative stress in preeclampsia and placental diseases. Int. J. Mol. Sci. 19, 1–29. https://doi.org/10.3390/ijms19051496.

Assibey-Mensah, V., Glantz, J.C., Hopke, P.K., Jusko, T.A., Thevenet-Morrison, K., Chalupa, D., Rich, D.Q., 2020. Wintertime wood smoke, traffic particle pollution, and preeclampsia. Hypertension 75, 851–858. https://doi.org/10.1161/HYPERTENSIONAHA.119.13139.

Bandyopadhyay, T., Bhatia, B.D., Khanna, H.D., 2017. A study of oxidative stress in neonates delivered through meconium-stained amniotic fluid. Eur. J. Pediatr. 176, 317–325. https://doi.org/10.1007/s00431-016-2845-0.

Bharadwaj, S., Bhat, V.B., Vickneswaran, V., Adhisivam, B., Zachariah, B., Habeebullah, S., 2018. Oxidative stress in preeclamptic mother – newborn dyads and its correlation with early neonatal outcome – a case control study. J. Matern. Fetal Neonatal Med. 31, 1548–1553. https://doi.org/10.1080/14767058.2017.1319933.

Bharadwaj, S.K., Vishnu Bhat, B., Vickneswaran, V., Adhisivam, B., Bobby, Z., Habeebullah, S., 2018. Oxidative stress, antioxidant status and neurodevelopmental outcome in neonates born to pre-eclamptic mothers. Indian J. Pediatr. 85, 351–357. https://doi.org/10.1007/s12098-017-2560-5.

Birben, E., Sahiner, U.M., Sackesen, C., Erzurum, S., Kalayci, O., 2012. Oxidative stress and antioxidant defense. World Allergy Organ. J. 5, 9–19. https://doi.org/10.1097/WOX.0b013e3182439613.

Buege, J.A., Aust, S.D., 1978. Microsomal Lipid Peroxidation, pp. 302–310 https://doi.org/10.1016/S0076-6879(78)52032-6.

Buonocore, G., Perrone, S., Tataranno, M.L., 2017. Oxidative stress in the newborn. Oxidative Med. Cell. Longev. 2017, 1–2. https://doi.org/10.1155/2017/1094247.

Burcham, P.C., 2007. Modified protein carbonyl assay detects oxidised membrane proteins: a new tool for assessing drug- and chemically-induced oxidative cell injury. J. Pharmacol. Toxicol. Methods 56, 18–22. https://doi.org/10.1016/j.vascn.2006.02.015.

Burton, G.J., Jauniaux, E., 2011. Oxidative stress. Best Pract. Res. Clin. Obstet. Gynaecol. 25, 287–299. https://doi.org/10.1016/j.bpobgyn.2010.10.016.

Casavant, S.G., Cong, X., Fitch, R.H., Moore, J., Rosenkrantz, T., Starkweather, A., 2019. Allostatic load and biomarkers of stress in the preterm infant: an integrative review. Biol. Res. Nurs. 21, 210–223. https://doi.org/10.1177/1099800418824415.

Chamy, V.M., Lepe, J., Catalán, Á., Retamal, D., Escobar, J.A., Madrid, E.M., 2006. Oxidative stress is closely related to clinical severity of pre-eclampsia. Biol. Res. 39. https://doi.org/10.4067/S0716-97602006000200005.

Chiarello, D.I., Abad, C., Rojas, D., Toledo, F., Vázquez, C.M., Mate, A., Sobrevia, L., Marín, R., 2020. Oxidative stress: normal pregnancy versus preeclampsia. Biochim. Biophys. Acta (BBA) - Mol. Basis Dis. 1866, 165354. https://doi.org/10.1016/j.bbadis.2018.12.005.

Choe, S.-A., Kauderer, S., Eliot, M.N., Glazer, K.B., Kingsley, S.L., Carlson, L., Awad, Y.A., Schwartz, J.D., Savitz, D.A., Wellenius, G.A., 2018. Air pollution, land use, and complications of pregnancy. Sci. Total Environ. 645, 1057–1064. https://doi.org/10.1016/j.scitotenv.2018.07.237.

Dadvand, P., Figueras, F., Basagaña, X., Beelen, R., Martinez, D., Cirach, M., Schembari, A., Hoek, G., Brunekreef, B., Nieuwenhuijsen, M.J., 2013. Ambient air pollution and preeclampsia: a spatiotemporal analysis. Environ. Health Perspect. 121, 1365–1371. https://doi.org/10.1289/ehp.1206430.

Dadvand, P., Ostro, B., Amato, F., Figueras, F., Minguillón, M.-C., Martinez, D., Basagaña, X., Querol, X., Nieuwenhuijsen, M., 2014. Particulate air pollution and preeclampsia: a source-based analysis. Occup. Environ. Med. 71, 570–577. https://doi.org/10.1136/oemed-2013-101693.

Dash, P., 2003. Nitric oxide protects human extravillous trophoblast cells from apoptosis by a cyclic GMP-dependent mechanism and independently of caspase 3 nitrosylation. Exp. Cell Res. 287, 314–324. https://doi.org/10.1016/S0014-4827(03)00156-3.

Dastoorpoor, M., Khanjani, N., Moradgholi, A., Sarizadeh, R., Cheraghi, M., Estebsari, F., 2021. Prenatal exposure to ambient air pollution and adverse pregnancy outcomes in Ahvaz, Iran: a generalized additive model. Int. Arch. Occup. Environ. Health 94, 309–324. https://doi.org/10.1007/s00420-020-01577-8.

de Almeida, V.O., Pereira, R.A., Amantéa, S.L., Rhoden, C.R., Colvero, M.O., 2021. Neonatal diseases and oxidative stress in premature infants: an integrative review. J. Pediatr. https://doi.org/10.1016/j.jped.2021.11.008.

de Souza Rugolo, L.M.S., Bentlin, M.R., Trindade, C.E.P., 2011. Preeclampsia: effect on the fetus and newborn. NeoReviews 12, e198–e206. https://doi.org/10.1542/neo.12-4-e198.

D'Souza, V., Rani, A., Patil, V., Pisal, H., Randhir, K., Mehendale, S., Wagh, G., Gupte, S., Joshi, S., 2016. Increased oxidative stress from early pregnancy in women who develop preeclampsia. Clin. Exp. Hypertens. 38, 225–232. https://doi.org/10.3109/10641963.2015.1081226.

Duhig, K., Chappell, L.C., Shennan, A.H., 2016. Oxidative stress in pregnancy and reproduction. Obstet. Med. 9, 113–116. https://doi.org/10.1177/1753495X16648495.

Falsaperla, R., Lombardo, F., Filosco, F., Romano, C., Saporito, M.A.N., Puglisi, F., Piro, E., Ruggieri, M., Pavone, P., 2020. Oxidative stress in preterm infants: overview of current evidence and future prospects. Pharmaceuticals 13, 145. https://doi.org/10.3390/ph13070145.

Feng, S., Gao, D., Liao, F., Zhou, F., Wang, X., 2016. The health effects of ambient PM2.5 and potential mechanisms. Ecotoxicol. Environ. Saf. 128, 67–74. https://doi.org/10.1016/j.ecoenv.2016.01.030.

Fu, L., Chen, Y., Yang, X., Yang, Z., Liu, S., Pei, L., Feng, B., Cao, G., Liu, X., Lin, H., Li, X., Ye, Y., Zhang, B., Sun, J., Xu, X., Liu, T., Ma, W., 2019. The associations of air pollution exposure during pregnancy with fetal growth and anthropometric measurements at birth: a systematic review and meta-analysis. Environ. Sci. Pollut. Res. 26, 20137–20147. https://doi.org/10.1007/s11356-019-05338-0.

García, L., 2016. Relación de la gravedad de la preeclampsia con su estado oxidativo relationship between oxidative stress and the severity of preeclampsia. Salud(i)Ciencia 22, 118–123.

Gitto, E., Marseglia, L., Manti, S., D'Angelo, G., Barberi, I., Salpietro, C., Reiter, R.J., 2013. Protective role of melatonin in neonatal diseases. Oxidative Med. Cell. Longev. 2013, 1–6. https://doi.org/10.1155/2013/980374.

Giuffrè, M., Rizzo, M., Scaturro, G., Pitruzzella, A., Gammazza, A.M., Cappello, F., Corsello, G., Li Volti, G., 2015. Oxidative stress markers at birth: analyses of a neonatal population. Acta Histochem. 117, 486–491. https://doi.org/10.1016/j.acthis.2015.01.007.

Gregory, K.E., DeForge, C.E., Natale, K.M., Phillips, M., Van Marter, L.J., 2011. Necrotizing enterocolitis in the premature infant. Adv. Neonatal Care 11, 155–164. https://doi.org/10.1097/ANC.0b013e31821baaf4.

Grevendonk, L., Janssen, B.G., Vanpoucke, C., Lefebvre, W., Hoxha, M., Bollati, V., Nawrot, T.S., 2016. Mitochondrial oxidative DNA damage and exposure to particulate air pollution in mother-newborn pairs. Environ. Health 15, 10. https://doi.org/10.1186/s12940-016-0095-2.

Guerby, P., Tasta, O., Swiader, A., Pont, F., Bujold, E., Parant, O., Vayssiere, C., Salvayre, R., Negre-Salvayre, A., 2021. Role of oxidative stress in the dysfunction of the placental endothelial nitric oxide synthase in preeclampsia. Redox Biol. 40, 101861. https://doi.org/10.1016/j.redox.2021.101861.

Gunzler, W., Flohe-Clairborne, A., 1985. Glutathione peroxidase. Handbook of Methods for Oxygen Radical Research. CRC Press, GreenWald, Boca Raton FL, pp. 285–290.

Halliwell, B., 2007. Biochemistry of oxidative stress. Biochem. Soc. Trans. 35, 1147–1150. https://doi.org/10.1042/BST0351147.

Hansson, S.R., NÃ¤Ã¤v, Ã., Erlandsson, L., 2015. Oxidative stress in preeclampsia and the role of free fetal hemoglobin. Front. Physiol. 5, 1–11. https://doi.org/10.3389/fphys.2014.00516.

Higgins, R.D., Jobe, A.H., Koso-Thomas, M., Bancalari, E., Viscardi, R.M., Hartert, T.V., Ryan, R.M., Kallapur, S.G., Steinhorn, R.H., Konduri, G.G., Davis, S.D., Thebaud, B., Clyman, R.I., Collaco, J.M., Martin, C.R., Woods, J.C., Finer, N.N., Raju, T.N.K., 2018. Bronchopulmonary dysplasia: executive summary of a workshop. J. Pediatr. 197, 300–308. https://doi.org/10.1016/j.jpeds.2018.01.043.

Hoffmann, B., Roebbel, N., Gumy, S., Forastiere, F., Brunekreef, B., Jarosinska, D., Walker, K.D., van Erp, A.M., O'Keefe, R., Greenbaum, D., Williams, M., Krzyzanowski, M., Kelly, F.J., Brauer, M., Bruyninckx, H., Boogaard, H., 2020. Air pollution and health: recent advances in air pollution epidemiology to inform the european green Deal: a joint workshop report of ERS, WHO,ISEE and HEI. Eur. Respir. J. 56, 2002575. https://doi.org/10.1183/13993003.02575-2020.

Hu, H., Ha, S., Xu, X., 2017. Ozone and hypertensive disorders of pregnancy in Florida: identifying critical windows of exposure. Environ. Res. 153, 120–125. https://doi.org/10.1016/j.envres.2016.12.002.

Hubel, C.A., Roberts, J.M., Taylor, R.N., Musci, T.J., Rogers, G.M., McLaughlin, M.K., 1989. Lipid peroxidation in pregnancy: new perspectives on preeclampsia. Am. J. Obstet. Gynecol. 161, 1025–1034. https://doi.org/10.1016/0002-9378(89)90778-3.

Jia, Y.-Y., Wang, Q., Liu, T., 2017. Toxicity research of PM2.5 compositions in vitro. Int. J. Environ. Res. Public Health 14, 232. https://doi.org/10.3390/ijerph14030232.

Jia, L., Liu, Q., Hou, H., Guo, G., Zhang, T., Fan, S., Wang, L., 2020. Association of ambient air pollution with risk of preeclampsia during pregnancy: a retrospective cohort study. BMC Public Health 20, 1663. https://doi.org/10.1186/s12889-020-09719-w.

Jiang, Z.-Y., Hunt, J.V., Wolff, S.P., 1992. Ferrous ion oxidation in the presence of xylenol orange for detection of lipid hydroperoxide in low density lipoprotein. Anal. Biochem. 202, 384–389. https://doi.org/10.1016/0003-2697(92)90122-N.

Kim, J.Y., Lee, E.Y., Choi, I., Kim, J., Cho, K., 2015. Effects of the particulate matter2.5 (PM2.5) on lipoprotein metabolism, uptake and degradation, and embryo toxicity. Mol. Cells 38, 1096–1104. https://doi.org/10.14348/molcells.2015.0194.

Knapen, M.F.C., Peters, W.H., Mulder, T.P., Merkus, H.M.W., Jansen, J.B.M., Steegers, E.A., 1999. Glutathione and glutathione-related enzymes in decidua and placenta of controls and women with pre-eclampsia. Placenta 20, 541–546. https://doi.org/10.1053/plac.1999.0408.

Kumar, C.A., Das, U.N., 2023. Lipid peroxides, anti-oxidants and nitric oxide in patients with pre-eclampsia and essential hypertension. Med. Sci. Monit. 6, 901–907.

Levine, R.L., Williams, J.A., Stadtman, E.P., Shacter, E., 1994. Carbonyl Assays for Determination of Oxidatively Modified Proteins, pp. 346–357 https://doi.org/10.1016/S0076-6879(94)33040-9.

Li, Z., Liu, Q., Xu, Z., Guo, X., Wu, S., 2020. Association between short-term exposure to ambient particulate air pollution and biomarkers of oxidative stress: a meta-analysis. Environ. Res. 191, 110105. https://doi.org/10.1016/j.envres.2020.110105.

Liang, L., Gong, P., Cong, N., Li, Z., Zhao, Y., Chen, Y., 2019. Assessment of personal exposure to particulate air pollution: the first result of City Health Outlook (CHO) project. BMC Public Health 19, 711. https://doi.org/10.1186/s12889-019-7022-8.

Liu, Linli, Zheng, B., Jiang, Z., Wu, S., Jin, Q., Lin, P., Lin, Z., 2020. Elevated Cord Blood Oxidative Stress Biomarkers Negatively Affect Neonatal Outcomes of Mothers With Severe

Preeclampsia: A Case-control Study, pp. 1–19 https://doi.org/10.21203/rs.3.rs-23080/v1.
Lorentzen, B., Henriksen, T., 1998. Plasma lipids and vascular dysfunction in preeclampsia. Semin. Reprod. Med. 16, 33–39. https://doi.org/10.1055/s-2007-1016250.
Mandakh, Y., Rittner, R., Flanagan, E., Oudin, A., Isaxon, C., Familari, M., Hansson, S.R., Malmqvist, E., 2020. Maternal exposure to ambient air pollution and risk of preeclampsia: a population-based cohort study in Scania, Sweden. Int. J. Environ. Res. Public Health 17, 1744. https://doi.org/10.3390/ijerph17051744.
Mandakh, Y., Oudin, A., Erlandsson, L., Isaxon, C., Hansson, S.R., Broberg, K., Malmqvist, E., 2021. Association of prenatal ambient air pollution exposure with placental mitochondrial DNA copy number, telomere length and preeclampsia. Front. Toxicol. 3. https://doi.org/10.3389/ftox.2021.659407.
Marseglia, L., D'Angelo, G., Manti, S., Arrigo, T., Barberi, I., Reiter, R.J., Gitto, E., 2014. Oxidative stress-mediated aging during the fetal and perinatal periods. Oxidative Med. Cell. Longev. 2014, 1–8. https://doi.org/10.1155/2014/358375.
Michikawa, T., Morokuma, S., Fukushima, K., Ueda, K., Takeuchi, A., Kato, K., Nitta, H., 2015. A register-based study of the association between air pollutants and hypertensive disorders in pregnancy among the Japanese population. Environ. Res. 142, 644–650. https://doi.org/10.1016/j.envres.2015.08.024.
Misra, H.P., Fridovich, I., 1972. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. J. Biol. Chem. 247, 3170–3175 https://doi.org/4623845.
Murki, S., 2014. Intrauterine growth retardation - a review article. J. Neonatal Biol. 03. https://doi.org/10.4172/2167-0897.1000135.
Mutinati, M., Pantaleo, M., Roncetti, M., Piccinno, M., Rizzo, A., Sciorsci, R., 2014. Oxidative stress in neonatology. A review. Reprod. Domest. Anim. 49, 7–16. https://doi.org/10.1111/rda.12230.
Nagiah, S., Phulukdaree, A., Naidoo, D., Ramcharan, K., Naidoo, R., Moodley, D., Chuturgoon, A., 2015. Oxidative stress and air pollution exposure during pregnancy. Hum. Exp. Toxicol. 34, 838–847. https://doi.org/10.1177/0960327114559992.
Negi, R., Pande, D., Karki, K., Kumar, A., Khanna, R.S., Khanna, H.D., 2012. Trace elements and antioxidant enzymes associated with oxidative stress in the pre-eclamptic/eclamptic mothers during fetal circulation. Clin. Nutr. 31, 946–950. https://doi.org/10.1016/j.clnu.2012.04.005.
Negi, R., Pande, D., Karki, K., Kumar, A., Khanna, R.S., Khanna, H.D., 2014. Association of oxidative DNA damage, protein oxidation and antioxidant function with oxidative stress induced cellular injury in pre-eclamptic/eclamptic mothers during fetal circulation. Chem. Biol. Interact. 208, 77–83. https://doi.org/10.1016/j.cbi.2013.11.010.
Negi, R., Pande, D., Karki, K., Kumar, A., Khanna, R.S., Khanna, H.D., 2015. A novel approach to study oxidative stress in neonatal respiratory distress syndrome. BBA Clin. 3, 65–69. https://doi.org/10.1016/j.bbacli.2014.12.001.
Nikolic, A., Cabarkapa, V., Novakov Mikic, A., Jakovljević, A., Stosic, Z., 2016. Ceruloplasmin and antioxidative enzymes in pre-eclampsia. J. Matern. Fetal Neonatal Med. 29, 2987–2993. https://doi.org/10.3109/14767058.2015.1111333.
Nobles, C.J., Williams, A., Ouidir, M., Sherman, S., Mendola, P., 2019. Differential effect of ambient air pollution exposure on risk of gestational hypertension and preeclampsia. Hypertension 74, 384–390. https://doi.org/10.1161/HYPERTENSIONAHA.119.12731.
Norishadkam, M., Andishmand, S., Zavar reza, J., Zare Sakhvidi, M.J., Hachesoo, V.R., 2017. Oxidative stress and DNA damage in the cord blood of preterm infants. Mutat. Res. Genet. Toxicol. Environ. Mutagen. 824, 20–24. https://doi.org/10.1016/j.mrgentox.2017.10.003.
Ozsurekci, Y., Aykac, K., 2016. Oxidative stress related diseases in newborns. Oxidative Med. Cell. Longev. 2016, 1–9. https://doi.org/10.1155/2016/2768365.
Parvez, S., Raisuddin, S., 2005. Protein carbonyls: novel biomarkers of exposure to oxidative stress-inducing pesticides in freshwater fish Channa punctata (Bloch). Environ. Toxicol. Pharmacol. 20, 112–117. https://doi.org/10.1016/j.etap.2004.11.002.
Pedersen, M., Stayner, L., Slama, R., Sørensen, M., Figueras, F., Nieuwenhuijsen, M.J., Raaschou-Nielsen, O., Dadvand, P., 2014. Ambient air pollution and pregnancy-induced hypertensive disorders: a systematic review and meta-analysis. Hypertension 64, 494–500. https://doi.org/10.1161/HYPERTENSIONAHA.114.03545.
Pedersen, M., Halldorsson, T.I., Olsen, S.F., Hjortebjerg, D., Ketzel, M., Grandström, C., Raaschou-Nielsen, O., Sørensen, M., 2017. Impact of road traffic pollution on pre-eclampsia and pregnancy-induced hypertensive disorders. Epidemiology 28, 99–106. https://doi.org/10.1097/EDE.0000000000000555.
Pereira, G., Haggar, F., Shand, A.W., Bower, C., Cook, A., Nassar, N., 2013. Association between pre-eclampsia and locally derived traffic-related air pollution: a retrospective cohort study. J. Epidemiol. Community Health 67, 147–152. https://doi.org/10.1136/jech-2011-200805.
Perrone, S., Tataranno, M.L., Negro, S., Longini, M., Marzocchi, B., Proietti, F., Iacoponi, F., Capitani, S., Buonocore, G., 2010. Early identification of the risk for free radical-related diseases in preterm newborns. Early Hum. Dev. 86, 241–244. https://doi.org/10.1016/j.earlhumdev.2010.03.008.
Perrone, S., Tataranno, M.L., Stazzoni, G., Buonocore, G., 2012. Oxidative stress and free radicals related diseases of the newborn. Adv. Biosci. Biotechnol. 03, 1043–1050. https://doi.org/10.4236/abb.2012.327127.
Perrone, S., Tataranno, M.L., Negro, S., Longini, M., Toti, M.S., Alagna, M.G., Proietti, F., Bazzini, F., Toti, P., Buonocore, G., 2016. Placental histological examination and the relationship with oxidative stress in preterm infants. Placenta 46, 72–78. https://doi.org/10.1016/j.placenta.2016.08.084.
Phaniendra, A., Jestadi, D.B., Periyasamy, L., 2015. Free radicals: properties, sources, targets, and their implication in various diseases. Indian J. Clin. Biochem. 30, 11–26. https://doi.org/10.1007/s12291-014-0446-0.
Pimentel, A.M.L., Pereira, R., Costa, C.A., Mann, G.E., Cordeiro, V.S.C., Moura, R.S.De, Brunini, T.M.C., 2013. L-arginine-nitric oxide pathway and oxidative stress in plasma and platelets of patients with pre-eclampsia. Hypertens. Res., 783–788 https://doi.org/10.1038/hr.2013.34.
Radi, R., Turrens, J.F., Chang, L.Y., Bush, K.M., Crapo, J.D., Freeman, B.A., 1991. Detection of catalase in rat heart mitochondria. J. Biol. Chem. 266, 22028–22034.
Roberts, J.M., Druzin, M., August, P.A., Gaiser, R.R., Bakris, G., Granger, J.P., Barton, J.R., Jeyabalan, A., Bernstein, I.a, Johnson, D.D., Karamanchi, S.A., Spong, C.Y., Lindheiner, M.D., Tsingas, E., Owens, M.Y., Martin Jr., J.N., Saade Jr., G.R., Sibai Jr., B.M., 2013. ACOG Guidelines: Hypertension in Pregnancy. American College of Obstetricians and Gynecologists https://doi.org/10.1097/01.AOG.0000437382.03963.88.
Romero-Guzmán, E.T., Hernández-Mendoza, H., Kuri-Cruz, A., Reyes-Gutiérrez, L.R., 2018. Airborne particulate material in Metropolitan Zone of Toluca Valley (Mexico) by SEM and ICP-SFMS. Chem. Ecol. 34, 482–494. https://doi.org/10.1080/02757540.2018.1433167.
Roy, S., Dhobale, M., Dangat, K., Mehendale, S., Lalwani, S., Joshi, S., 2015. Differential oxidative stress levels in mothers with preeclampsia delivering male and female babies. J. Matern. Fetal Neonatal Med. 28, 1973–1980. https://doi.org/10.3109/14767058.2014.974537.
Rudra, C.B., Williams, M.A., Sheppard, L., Koenig, J.Q., Schiff, M.A., 2011. Ambient carbon monoxide and fine particulate matter in relation to preeclampsia and preterm delivery in Western Washington State. Environ. Health Perspect. 119, 886–892. https://doi.org/10.1289/ehp.1002947.
Sanchez-Aranguren, L.C., Prada, C.E., RiaÃ ± o-Medina, C.E., Lopez, M., 2014. Endothelial dysfunction and preeclampsia: role of oxidative stress. Front. Physiol., 5 https://doi.org/10.3389/fphys.2014.00372.
Savitz, D.A., Elston, B., Bobb, J.F., Clougherty, J.E., Dominici, F., Ito, K., Johnson, S., McAlexander, T., Ross, Z., Shmool, J.L.C., Matte, T.D., Wellenius, G.A., 2015. Ambient fine particulate matter, nitrogen dioxide, and hypertensive disorders of pregnancy in New York City. Epidemiology 26, 748–757. https://doi.org/10.1097/EDE.0000000000000349.
Schoots, M.H., Gordijn, S.J., Scherjon, S.A., van Goor, H., Hillebrands, J.-L., 2018. Oxidative stress in placental pathology. Placenta 69, 153–161. https://doi.org/10.1016/j.placenta.2018.03.003.
Shaarawy, M., Aref, A., Emad Salem, M., Sheiba, M., 1998. Radical-scavenging antioxidants in pre-eclampsia and eclampsia. Int. J. Gynecol. Obstet. 60, 123–128. https://doi.org/10.1016/S0020-7292(97)00256-7.
Silva, A.B.da, Medeiros, J.F.P., Lima, M.S.R., Mata, A.M.B.da, Andrade, E.D.de O., Bezerra, D.S., Osório, M.M., Dimenstein, R., Ribeiro, K.D.da S., 2019. INTRAUTERINE GROWTH AND THE VITAMIN E STATUS OF FULL-TERM AND PRETERM NEWBORNS. Rev. Paul. Pediatr. 37, 291–296. https://doi.org/10.1590/1984-0462/;2019;37;3;00003.
Sinha, N., Dabla, P., 2015. Oxidative stress and antioxidants in hypertension–a current review. Curr. Hypertens. Rev. 11, 132–142. https://doi.org/10.2174/1573402111666150529130922.
Soma-Pillay, P., Nelson-Piercy, C., Tolppanen, H., Mebazaa, A., 2016. Physiological changes in pregnancy. Cardiovasc. J. Afr. 27, 89–94. https://doi.org/10.5830/CVJA-2016-021.
Stephensen, E., 2000. Biochemical indicators of pollution exposure in shorthorn sculpin (Myoxocephalus scorpius), caught in four harbours on the southwest coast of Iceland. Aquat. Toxicol. 48, 431–442. https://doi.org/10.1016/S0166-445X(99)00062-4.
Sun, M., Yan, W., Fang, K., Chen, D., Liu, J., Chen, Y., Duan, J., Chen, R., Sun, Z., Wang, X., Xia, Y., 2020. The correlation between PM2.5 exposure and hypertensive disorders in pregnancy: a meta-analysis. Sci. Total Environ. 703, 134985. https://doi.org/10.1016/j.scitotenv.2019.134985.
Taravati, A., Tohidi, F., 2018. Comprehensive analysis of oxidative stress markers and antioxidants status in preeclampsia. Taiwan. J. Obstet. Gynecol. 57, 779–790. https://doi.org/10.1016/j.tjog.2018.10.002.
Tenório, M.B., Ferreira, R.C., Moura, F.A., Bueno, N.B., de Oliveira, A.C.M., Goulart, M.O.F., 2019. Cross-talk between oxidative stress and inflammation in preeclampsia. Oxidative Med. Cell. Longev. 2019, 1–26. https://doi.org/10.1155/2019/8238727.
The American College of Obstetricians and Gynecologists, 2019. Clinical Management Guidelines for Obstetrician – Gynecologists Gestational Hypertension and Preeclampsia. 133, pp. 1–25.
Volpe, J.J., 1989. Intraventricular hemorrhage and brain injury in the premature infant.Neuropathology and pathogenesis. Clin. Perinatol. 16, 361–386.
Wang, Q., Zhang, H., Liang, Q., Knibbs, L.D., Ren, M., Li, C., Bao, J., Wang, S., He, Y., Zhu, L., Wang, X., Zhao, Q., Huang, C., 2018. Effects of prenatal exposure to air pollution on pre-eclampsia in Shenzhen, China. Environ. Pollut. 237, 18–27. https://doi.org/10.1016/j.envpol.2018.02.010.
Yang, C.-C., Tang, P.-L., Liu, P.-Y., Huang, W.-C., Chen, Y.-Y., Wang, H.-P., Chang, J.-T., Lin, L.-T., 2018. Maternal pregnancy-induced hypertension increases subsequent neonatal necrotizing enterocolitis risk. Medicine 97, e11739. https://doi.org/10.1097/MD.0000000000011739.
Yuan, L., Zhang, Y., Wang, W., Chen, R., Liu, Y., Liu, C., Kan, H., Gao, Y., Tian, Y., 2020. Critical windows for maternal fine particulate matter exposure and adverse birth outcomes: the Shanghai birth cohort study. Chemosphere 240, 124904. https://doi.org/10.1016/j.chemosphere.2019.124904.
Zha, Q.Bin, Yao, Y.F., Ren, Z.J., Li, X.J., Tang, J.H., 2017. Extracellular vesicles: an overview of biogenesis, function, and role in breast cancer. Tumor Biol. 39, 101042831769118. https://doi.org/10.1177/1010428317691182.