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Mercury-induced Oxidative Stress May Adversely Affect Pregnancy Outcome among Dental Staff: A Cohort Study

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Abstract

Background: Dental staff may be at increased risk of adverse pregnancy outcome secondary to their chronic exposure to mercury.

Objective: To investigate obstetric outcome among dental staff and explore the oxidative stress induced by mercury exposure.

Methods: A cohort of 64 pregnant dental staff (exposed group) and 60 pregnant employees (non-exposed group) were studied. Urinary mercury level and blood antioxidant activity were measured. Participants were followed to assess their obstetric outcome.

Results: The exposed group had a higher mean urinary mercury level and a lower blood antioxidant activity during the three trimesters compared to non-exposed group ($p<0.001$). Women in the exposed group were experienced more frequently spontaneous abortion and pre-eclampsia ($p<0.05$). Babies born to the women in the exposed group tended to be smaller for gestational age compared to those of non-exposed group ($p<0.001$).

Conclusion: Pregnant dental staff suffered higher odds of developing spontaneous abortion and pre-eclampsia and giving birth to babies smaller for gestational age. This may be linked to oxidative stress induced by exposure to mercury.

Keywords: Dental staff; Pregnancy outcome; Mercury poisoning; Oxidative stress; Antioxidants; Glutathione peroxidase; Superoxide dismutase

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Introduction

Mercury has been used for over two centuries as a dental restorative filling material. Despite worldwide repeated safety concerns, dental amalgam is still used in low- and middle-income countries as its alternatives are more expensive and less durable.[1-3] Dental staff members are constantly exposed to mercury vapor, which is readily absorbed through the skin and lungs and excreted by the kidneys.[4,5]

Adverse pregnancy outcome has been reported in previous studies with increased rates of spontaneous abortion and congenital malformations among women working in dental clinics.[6] This finding is, however, contradicted by other studies.[7,8] A cross-sectional study investigated the effect of elemental mercury exposure on antioxidative enzymes activities, as a pos-

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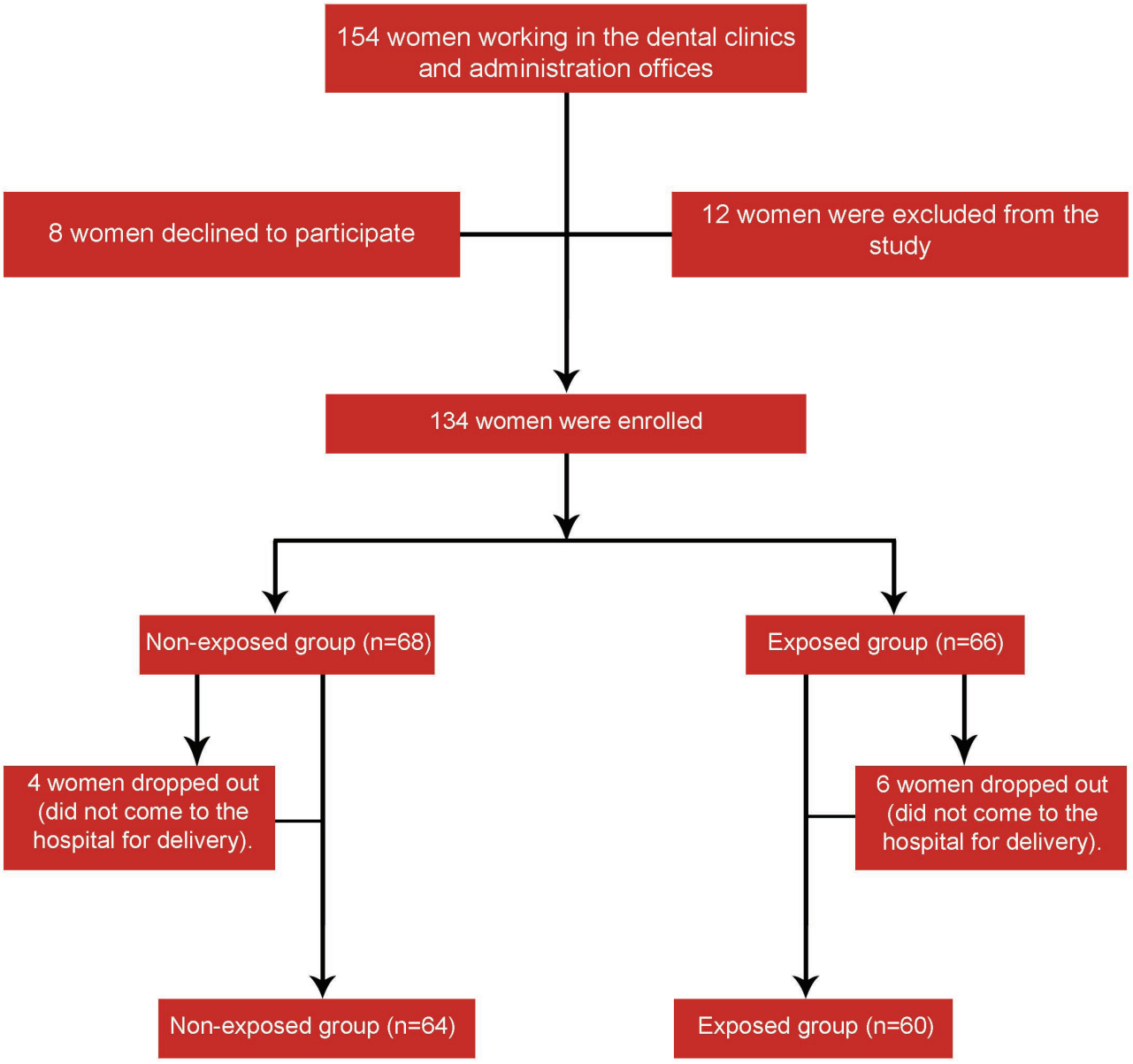

Figure 1: Flow diagram of recruitment and retention of participants in the study

sible mechanism of renal affection among dental staff, and reported decreased activity of glutathione peroxidase and superoxide dismutase in the blood of the exposed staff.[9]

The objective of this study was to investigate prospectively obstetric outcome among dental staff and to explore the oxidative stress induced by mercury exposure.

Materials and Methods

This cohort study was carried out at the Department of Public Health and Community Medicine in collaboration with the Departments of Obstetrics and Gynecology and Pediatrics, Menoufia Faculty of Medicine, Menoufia governorate, Egypt,

between January, 2016 and August, 2017, the date of the last follow-up of the last enrolled participant.

Participants

All pregnant women in the first trimester who were working at Dental Departments at Shibin El-Kom teaching hospital and 11 Central hospitals in Menoufia governorate (served as study or exposed group), and pregnant employees in the hospital administration offices (served as non-exposed group), were invited to participate in the study.

Women with medical conditions such as diabetes mellitus and hypertension, chronic alcohol abuse, multi-fetal (twins and triplets) pregnancies, obesity, exposure to cigarette smoke (active or passive), living in rural areas with potential exposure to pesticides, poor housing, and living within one kilometer in an area of cell phone base transceiver station (BTS) were excluded from the study.

After exclusion of non-responders and those who did not fulfill the inclusion criteria, 64 exposed dental staff and 60 non-exposed employees were left for in the study (Fig 1).

Participants were interviewed between 9:00 and 14:00 by two trained investigators at the Dental Clinic or at their work offices where demographic, medical and occupational data were collected. The participants were asked to attend the Obstetrics and Gynecology outpatient clinic, Menoufia University hospital for antenatal care visits every 2-4 weeks throughout their pregnancy and to deliver at the same hospital to assess their obstetric outcome.

Mercury Level

Participants were instructed to abstain from eating fish or taking any food supplements containing omega fatty acids prior to the assessment of urinary mercury to avoid false increase in the mercury values.

TAKE-HOME MESSAGE

- Pregnant dental staff carried a higher risk of spontaneous abortion, pre-eclampsia.
- Babies born to female dental staff were smaller for gestational age.
- These might be due to oxidative stress induced by exposure to mercury.

Measurement of urinary mercury was performed three times, in every pregnancy trimester. Participants were asked to bring 20–40 mL of their morning urine sample in a clean plastic container without glued cap cover. Samples were kept at -4 °C to be analyzed later for the presence of inorganic mercury, using spectrophotometric cold vapor-atomic absorption at the institute of measurements and calibration, Cairo, Egypt. Results were expressed as µg mercury/g of urinary creatinine to alleviate variations in urine physical characteristics.

Environmental mercury levels were measured in the Dental clinics using a mercury vapor analyzer ELTWI-"MS" (survey mode) three times in accordance with urinary mercury measurements. Three readings were taken every time at each Dental clinic and the mean values were calculated.

Enzymes Activities

The blood glutathione peroxidase and superoxide dismutase activities were measured at the initial enrollment of the participant into the study. Measurement of erythrocyte activity of superoxide dismutase was done using xanthine oxidase enzyme via enzymatic method[10] (Randox kit, USA); glutathione peroxidase activity of erythrocytes lysate was determined using hydrogen peroxide method[11] (Randox kit, USA).

Table 1: Maternal baseline characteristics. Values are mean (SD) or median [IQR].

Parameter	Exposed group (n=64)	Non-exposed group (n=60)
Age (yrs)	25.6 (4.2)	25.9 (4.5)
Parity	2 [1 to 3]	2 [1 to 3]
Body mass index (kg/m²)	22.2 (2.4)	22.8 (2.7)
Duration of employment (yrs)	7.6 (4.3)	7.2 (4.8)

None of the variables was significantly different between the studied groups.

Outcome Measures

Maternal outcome

Maternal outcomes considered included having abortion, defined as interruption (threatened abortion) or termination of pregnancy (either spontaneous or induced) before the 20th week of pregnancy; development of pre-eclampsia; mode of delivery; post-partum hemorrhage (PPH); and defective lactation. Pre-eclampsia was defined as a new-onset hypertension (systolic blood pressure of ≥140 mm Hg and/or diastolic blood pressure of ≥90 mm Hg) after 20th week of gestation recorded on two occasions four hours apart associated with new-onset proteinuria (≥0.3 g of protein in 24-hour urine or urinary dipsticks ≥1+).

Table 2: Measurements of Urinary mercury and Antioxidant activity in blood. Values are mean (SD).

Parameter	Exposed group (n=64)	Non-exposed group (n=60)
Urinary mercury (µg/g Cr*)		
1st trimester	42.2 (14.6)	6.2 (3.8)
2nd trimester	41.8 (15.3)	6.3 (3.7)
3rd trimester	42.8 (13.7)	7.1 (3.9)
Antioxidant activity		
Glutathione peroxidase (U/g Hb†)	48.1 (6.6)	66.4 (5.4)
Superoxide dismutase (U/g Hb)	688.4 (87.6)	822.6 (66.4)

All of the variables were significantly (p<0.001) different between the studied groups, *Creatinine, †Hemoglobin

Fetal and neonatal outcome

Fetal and neonatal outcomes considered included having congenital malformations; being small for gestational age (SGA), defined as a birth weight <5th percentile; prematurity (delivery before the 37th week of gestation); presence of placental abruption; intrauterine fetal demise (IUFD); admission to neonatal intensive care unit (NICU); and neonatal death, defined as death during the first four weeks after delivery.

Ethics

The Ethical Committee for medical research at Menoufia Faculty of Medicine reviewed and formally approved the study protocol before commencement of the study. All participants signed an informed consent form after thorough explanation of the study objectives. The reported investigations were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2000.

Statistical Analysis

Data were analyzed with SPSS® ver 22 for Windows® (SPSS Inc, Chicago, IL, USA). *Student's t* test was used for comparing means of two normally distributed continuous variables. *Mann-Whitney U* test was used for non-parametric variables. Chi square and Fischer's exact tests were used for comparison of categorical variables. A p value <0.05 was considered statistically significant.

Results

The highest mean environmental mercury levels recorded in each trimester were 18.0 (SD 0.9) µg/m³ for the first trimester, 19.0 (0.2) for the second, and 17.0 (0.6) µg/m³ for the third trimester.

Table 3: The frequency of maternal outcomes assessed

Outcome	Exposed group (n=64), n (%)	Non-exposed group (n=60), n (%)	RR* (95% CI)
Abortion	18 (28)	6 (10)	3.52 (1.29 to 2.23)
Threatened	3 (5)	2 (3)	
Spontaneous	8 (13)	2 (3)	
Induced	7 (11)	2 (3)	
Pre-eclampsia	16 (25)	5 (8)	3.67 (1.25 to 10.76)
Preterm labor	6 (9)	8 (13)	0.67 (0.22 to 2.07)
Cesarean section delivery	8 (13)	10 (17)	0.71 (0.26 to 1.95)
Post-partum hemorrhage	4 (6)	3 (5)	1.27 (0.27 to 5.9)
Defective lactation	6 (9)	8 (13)	0.67 (0.22 to 2.07)

*Crude relative risk calculated based on χ^2 or Fisher's exact test

There was no significant difference between the studied groups in terms of age, parity, body mass index, and duration of employment (Table 1). The exposed group had a significantly ($p<0.001$) higher mean urinary mercury level measured in the three trimesters and lower blood antioxidant enzymes activity compared to the non-exposed group (Table 2).

Women in the exposed group more frequently experienced spontaneous abortion (RR 3.52, 95% CI 1.29 to 2.23) and pre-eclampsia (RR 3.67, 95% CI 1.25 to 10.76) compared to the non-exposed group ($p<0.001$). No significant difference was observed between the studied groups in terms of preterm labor, delivery by Cesarean section, post-partum hemorrhage, and defective lactation (Table 3).

Babies born to women in the exposed group tended to be smaller for gestational age (RR 6.2, 95% CI 2.3 to 16.4) compared to the non-exposed group ($p<0.001$). No significant difference was observed between both groups in terms of the frequency of congenital malformations, intrauterine fetal demise, admission to NICU and neonatal death (Table 4).

Discussion

A higher frequency of adverse pregnancy

Table 4: The frequency of fetal and neonatal outcomes assessed

Outcome	Exposed group (n=64), n (%)	Non-exposed group (n=60), n (%)	RR* (95% CI)
Congenital malformations	2 (3)	2 (3)	0.94 (0.13 to 6.8)
Small for gestational age	26 (41)	6 (10)	6.2 (2.3 to 16.4)
Intrauterine fetal demise	0 (0)	0 (0)	—
Admission to neonatal ICU	6 (9)	6 (10)	0.93 (0.28 to 3.06)
Neonatal mortality	0 (0)	0 (0)	—

*Crude relative risk calculated based on χ^2 or Fisher's exact test

outcome was observed among female dental staff members who were exposed to mercury. Mercury has been reported to increase the oxidative stress via decreasing the activity of two major antioxidant enzymes, namely glutathione peroxidase and superoxide dismutase; the increase was correlated with duration of occupational exposure.[9]

The rate of spontaneous abortion in clinical pregnancies is about 15%–20%. Previous hypotheses postulated that oxidative stress may induce endothelial damage and impair placental vascularization with subsequent spontaneous abortion.[12,13]

Although epidemiological link between spontaneous abortion and increasing maternal age, smoking, alcohol consumption, use of coffee, and history of previous spontaneous abortion has been reported,[14] we excluded women with such contributing factors from this study.

A recent study has demonstrated a link between compensated oxidative stress and spontaneous abortion in women with early spontaneous pregnancy loss compared to normal women with ongoing pregnancy.[15]

High metabolism and oxidative stress are frequent processes in the placenta. However, an imbalance between the protective and destructive mechanisms within the placenta seems to be linked with pregnancy-related disorders such as abortion, pre-eclampsia, and intrauterine growth restriction.[16]

A large-scale retrospective study reveals no increase in the observed frequency of congenital malformations, low-birth weight, preterm birth, small for gestational age, stillbirth, or prenatal death among female dental staff working in Norway from 1967 to 2006 compared to the general population.[17] This study was, however, retrospective with no available data on the occupational exposure or environmental measures related to mercury.

The poor obstetric outcome observed in our study among dental staff might be attributed to work practices leading to high mercury levels; in some clinics the amalgam was mixed by hand, while in others it was done by heating the mercury with subsequent release of vapor. Protective measures for reducing the exposure by cleaning up spills, and by using premixed amalgam should thus be implemented.

A recent study reports the association between exposure to methyl-mercury and higher blood pressure during pregnancy.[18] Also, a recent review links mercury toxicity with hypertension through several mechanisms including increases in oxidative stress and inflammation, reductions in oxidative defense, thrombosis, and mitochondrial dysfunction, depolarization, and autoxidation of the inner mitochondrial membrane.[19]

The strength of this study resides in being prospective in nature with assessment of occupational exposure to mercury which was also favored by environmental measurements. Inability to withdraw female dental staff from further exposure to mercury during pregnancy, which was impractical and reluctance to prescribe antioxidant drugs to them as well as non-repetition of antioxidant tests in the second and third trimesters of pregnancy secondary to their high costs, constitute the main limitations of this study. However, systematic reviews failed to demonstrate any beneficial effects of the use of antioxidants during pregnancy to decrease the occurrence of abortion, pre-eclampsia, or fetal growth restriction in the general or high risk population.[20,21]

In conclusion, pregnant dental staff carried a higher risk of spontaneous abortion, and pre-clampsia, and gave birth to smaller-for-gestational-age babies, which may be linked to oxidative stress induced by the exposure to mercury. Larger studies are encouraged to enforce or refute these findings.

Conflicts of Interest: None declared.

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