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Exposure to metals and congenital anomalies: A biomonitoring study of pregnant Bedouin-Arab women

Isabella Karakis [a,b,g], Daniella Landau [b,c], Maayan Yitshak-Sade [b,h], Reli Hershkovitz [b,d], Michal Rotenberg [e], Batia Sarov [b], Itamar Grotto [a,b,f], Lena Novack [b,*]

[a] Environmental Epidemiology Department, Ministry of Health, Jerusalem, Israel
[b] Faculty of Health Science, Ben-Gurion University of the Negev, Beer-Sheva, Israel
[c] Department of Neonatology, Soroka University Medical Center, Beer-Sheva, Israel
[d] Ultrasound Unit, Department of Obstetrics and Gynecology, Soroka University Medical Center, Beer-Sheva, Israel
[e] Laboratory of Clinical Toxicology and Pharmacology, Sheba Medical Center, Tel-Hashomer, Israel
[f] Public Health Services, Ministry of Health, Jerusalem, Israel
[g] Department of Public Health, The Ashkelon Academic College, Ashkelon, Israel
[h] Clinical Research Center, Soroka University Medical Center, Beer-Sheva, Israel

HIGHLIGHTS

- Almost a third of the pregnant women had a detectable metal in their urine.
- Aluminum and Arsenic were the most prevalent metals in urine.
- The study investigates pregnant women exposed to a hazardous environment.
- Household exposure was most highly associated with the detection of metals in urine.
- Impact is specific to a metal: Al–anomalies, As - preterm birth and lower weight.

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ABSTRACT

Background: The Bedouin-Arab population in Israel comprises a low socio-economic society in transition. Smoking among males and consanguineous marriages are frequent. A previous study showed elevated rates of major malformations within groups from this population residing near an industrial park, where high ambient values of arsenic (As) and nickel (Ni) were detected, compared to groups living in remote localities.
Objectives: We estimated the extent of exposure to metals in pregnant Bedouin-Arab women in relation to congenital malformations.
Methods: We collected maternal urine samples from 140 Bedouin women who gave birth in a local hospital. Patient medical history, type of marriage (consanguineous or non-consanguineous), and parental exposure history were collected by interview and medical records.
Results: Aluminum (Al) was detected in 37 women (26.4%), cadmium (Cd) in 2 (1.4%), As in 10 (7.1%), and Ni in 1 woman (0.7%). The detected rate of Cd exposure was low, though more than 92% of the fathers reported smoking. Concentrations of Al were higher for women residing within 10 km of the local industrial park (Prevalence Ratio (PR) = 1.12, p-value = 0.012) or who reported using a wood burning stove (PR = 1.37, p-value = 0.011) and cooking over an open fire (PR = 1.16, p-value = 0.076).
Exposure to Al was adversely associated with minor anomalies (OR = 3.8, p-value = 0.046) after adjusting for history of abortions (OR = 6.1, p-value = 0.007). Fetuses prenatally exposed to As were born prematurely (p-value = 0.001) and at lower weights (pv = 0.023).
Conclusions: The study population of pregnant women is exposed to high levels of metals mainly of household origin. Our findings may be generalized to similar populations in developing countries.

1. Introduction

The Bedouin-Arab population in Israel is characterized by a high rate of congenital malformations in comparison to the country's Jewish and

* Corresponding author at: Department of Public Health, Faculty of Health Sciences, POB 653, Ben-Gurion University, Beer-Sheva 84105, Israel.
E-mail address: novack@bgu.ac.il (L. Novack).

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other Arab populations (Bentov et al., 2006). In southern Israel, the Bedouin-Arab population numbers around 200,000 inhabitants, most of who are of low socio-economic level owing to their high rate of unemployment and generally low education level (The Central Bureau of Statistics in Israel). Consanguineous marriages, i.e., marriages within a family between first, second or third cousins, are estimated at 45% (Jaber et al., 1994; Jaber and Halpern, 2006). Half of the Bedouin population resides in traditional tribal settlements, where they live in temporary shacks or tents that do not afford sufficient protection from ambient air pollution. In addition, cooking and heating is often by open fire. While about 90% of Bedouin men smoke, the habit is much less common (10%) among Bedouin women (Jaber et al., 1994).

Being essentially unprotected from outdoor pollution, the Bedouin-Arab population is potentially exposed to the emissions of the local industrial park (IP), which comprises 24 chemical and pharmaceutical facilities and an incinerator, and which serves as the principal industrial waste disposal site for the entire country. The list of emissions from the chemical plants and evaporation pools includes a variety of aliphatic, aromatic and polycyclic hydrocarbons and a few dozen nonorganic agents, including heavy metals. The 2010 periodic report based on monitor readings of IP emissions showed high values for arsenic (As) and nickel (Ni) (Ecological Laboratories, 2012). The report also showed the presence of cadmium (Cd) and aluminum (Al), which in combination with other elements have known toxicological effects and are detrimental to human development. The presence of other measured chemical elements, e.g., lead, was minimal.

A study in southern Israel in 2006 indicated increased rates of major congenital malformations (MCMs) among Bedouin-Arab newborns whose mothers lived within 20 km of an IP when compared to Bedouin-Arab newborns residing in remote localities (5.6% vs. 4.8%, respectively, $p < 0.01$), suggesting an adverse impact of IP proximity on the levels of MCMs observed in the Bedouin population (Sarov et al., 2003). In this study, differences in the rates of MCMs as a function of distance were unlikely to be explained by the utilization of different health care services or by variations in the rates of consanguineous marriages.

The etiology of malformations is poorly understood and is believed to be a product of independent effects or a combination of genetic factors, medications, behavioral, occupational and/or environmental exposures (Wigle et al., 2008). The pregnancy period deemed the most sensitive and with the most potential for the induction of birth defects has been identified as 3–8 weeks of gestation (Mattison, 2010), but during the second trimester, the fetus is also considered highly sensitive to environmental exposure (Lacasana et al., 2005; Kim et al., 2007).

Developmental diseases of the embryo, among which are neural tube defects (Brender et al., 2006), have been related to the exposure to heavy and semi-heavy metals, as shown mostly in animal models (Lopez et al., 2008; Martinez et al., 2004; Robinson et al., 2009, 2010). Sources of exposure to metals include industry, the home environment, health behavior and nutritional and dietary habits. Exposure to heavy metals can be assessed using epigenetic channels (Ho et al., 2012). Specifically, heavy metal exposure is believed to cause oxidative stress that, in turn, may explain the future development of chronic and acute disorders (Cortessis et al., 2012). Some examples of birth defects in humans related to exposure to metals were found in studies reporting the adverse effects of tobacco on fetal development, partially due to the exposure to the toxic heavy metals contained in cigarette smoke (Rogers, 2009). An ecological study in China, where the distribution of geophysical elements in soil, water and food was compared between a province with an unusually high rate of birth defects and a control area, indicated that metals, specifically higher sulfur and lower strontium and aluminum levels, were associated with congenital malformations (Yu and Zhang, 2011).

The association of congenital malformations with the exposure to metals in pregnancy has been based mostly on ambient assessments of contaminated air distribution, but not on individual, biological measurements. The current study is the first attempt to assess the contribution of prenatal exposure to heavy and semi-heavy metals in pregnancy (further referred as "metals") to a clinical expression of malformations diagnosed at birth.

2. Objectives

We aimed to 1) investigate individual concentrations of metals in a population of pregnant women of Bedouin-Arab origin, and 2) analyze the association of metal levels in maternal urine at delivery with environmental exposures during pregnancy and congenital malformations and other birth outcomes in their fetuses and newborn infants.

We hypothesized that adverse environmental exposures will increase levels of metal concentrations in urine and that the increased exposure to metals at the time of the study will be associated with higher neonatal morbidity.

3. Methods

We focused our investigation on Cd, Ni, Al and As. Ni and Al were chosen for investigation based on the above-mentioned periodic report (Ecological Laboratories, 2012), whereas Cd was chosen due to the high prevalence of smoking among Bedouin-Arab males. We included As because it may be released from the open fires used for cooking and heating and due to the widespread use of pesticides among the Bedouin. Although lead was previously linked as a risk factor for congenital anomalies (Brender et al., 2006), it was not tested in the current study in view of its relatively low levels according to an official government report that reviewed the extent of lead pollution in Israel in the 1990s (Foner, 1999) and to a study of lead levels in teeth conducted around the same time (Bercovitz et al., 1993). The overall low level of lead in the country corresponds with the severe restrictions put in place, in the form of local regulations, for the use of this chemical in the color and toy industries.

3.1. Study population

During June–December 2013, we enrolled women upon their arrival to the Obstetric Emergency Department (OED) of the Soroka University Medical Center in Beer-Sheva, a tertiary medical center in southern Israel where all the births in the region take place. We included mothers of Bedouin-Arab origin who resided in Bedouin-Arab localities in the Negev. Only singleton deliveries were included. Newborns/fetuses were excluded if: (a) their gestational age was under 22 weeks; (b) birth weight was under 500 g; (c) delivery took place on the way to the hospital; (d) conditions precluded collection of a sterile urine sample, e.g., bleeding or rupture of membranes prior to arrival in OED; or (e) maternal age < 18 years.

Eligible women were approached by a trained, Arabic-speaking interviewer in the OED during the day shift on working days. Women were provided with explanations about the study and were invited to consent to participate in the study.

3.2. Sample collection and testing

Spot urine samples were collected in sterile 120-mL specimen containers. All urine samples were maintained at 4 °C for a maximum of 48 h and later frozen at −20 °C until shipment to the toxicology laboratory at the Sheba Medical Center in Tel-Hashomer, Israel, for analysis. To increase testing efficiency, we sampled mothers of fetuses with malformations, which artificially increased the proportion of anomalies analyzed in the study. Moreover, if the study hypothesis proves to be true, i.e., malformations are associated with exposure to metals, the values of metals in urine will be overestimated to a certain extent in our study.