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Environmental Research

journal homepage: www.elsevier.com/locate/envres

Exposure to arsenic in tap water and gestational diabetes: A French semiecological study



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ARTICLE INFO

Keywords: Arsenic in tap water Gestational diabetes mellitus *in utero* exposure Pre-pregnancy body mass index Semi-ecological study

ABSTRACT

Introduction: The increase in the prevalence of gestational diabetes mellitus (GDM) and its consequences for mother and children prompts research on their risk factors including environmental factors. Studies on exposure to arsenic (As) in tap water and the risk of GDM have not provided conclusive evidence, particularly when levels of exposure were low (from 10 to 50 μ g As/L). The main objective of this study was to assess the association between exposure to As in tap water and the risk of GDM.

Methods: A semi-ecological study was conducted from births recorded at the University Hospital of Clermont-Ferrand, France, in 2003, 2006 and 2010. Individual medical/obstetric data were available. As exposure was estimated from the concentrations of As measured during sanitary control of tap water supplied in the mothers' commune of residence (aggregate data). French guidelines for As in tap water were used to identify groups potentially exposed, designated "As +" (\geq 10 µg As/L) and "As -" (< 10 µg As/L). Multivariate logistic regression analysis was performed.

Results: 5053 women (5.7% with a GDM) were included. Overall, women in the As + group had a higher risk of GDM than those in the As - group (adjusted OR = 1.62; 95%CI: 1.01-2.53). Stratified analysis of pre-pregnancy body mass index (BMI) showed a positive association only for obese or overweight women (adjusted OR = 2.30; 95%CI: 1.13-4.50).

Conclusion: This French semi-ecological study provides additional arguments for an association between As exposure and the risk of GDM in particular in a context of low exposure. Further studies are needed to assess a potential interaction between As exposure and body mass index.

1. Introduction

Gestational diabetes mellitus (GDM) is defined by the World Health Organization (WHO) as "carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy" (Alberti and Zimmet, 1998). It is the cause of multiple longand short-term adverse outcomes both for the mother (such as increased incidence of caesarean sections and postpartum bleeding, and also type 2 diabetes and cardiovascular disease after pregnancy) and the child (such as risk of macrosomia, hypoglycaemia or neonatal hypocalcaemia, obesity and long-term type 2 diabetes) (Baz et al., 2016; HAPO Study Cooperative Research Group et al., 2008). The incidence of GDM worldwide currently ranges according to country from 2% to 13% (Audipog, 2017; Hunt and Schuller, 2007) and is steadily increasing (Lavery et al., 2017). Prevalence in France rose from 2.0% in 1994–1996 to 6.8% in 2012 (Audipog, 2017). This increase can be

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https://doi.org/10.1016/j.envres.2017.11.016

Abbreviations: As, arsenic; Audipog, Association des utilisateurs de dossiers informatisés en pédiatrie, obstétrique et gynécologie (Association of users of computer records in paediatrics, obstetrics and gynaecology); BMI, body mass index; CNGOF, Collège national des gynécologues et obstétriciens français (French National College of Gynaecologists and Obstetricians); GDM, Gestational diabetes mellitus; iAs, inorganic arsenic; OGTT, oral glucose tolerance test; SISE-Eaux, Système d'Information en Santé-Environnement sur les Eaux (Information System for Water, Environment and Health); WHO, World Health Organization

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Received 19 July 2017; Received in revised form 9 November 2017; Accepted 10 November 2017 0013-9351/ @ 2017 Elsevier Inc. All rights reserved.

partly explained by improved screening for associated disorders and greater prevalence of known risk factors such as maternal age and overweight (Hunt and Schuller, 2007; Lavery et al., 2017). Certain authors have also pointed to the role of environmental contaminants in the development of GDM (Arrebola et al., 2015; Robledo et al., 2015; Shapiro et al., 2015). Exposure to certain metals and metalloids, including arsenic (As), has been posited as one of those factors (Ettinger et al., 2009; Farzan et al., 2016; Peng et al., 2015; Shapiro et al., 2015).

As, which is naturally present in the earth's crust, is a water contaminant in numerous countries including Bangladesh, Taiwan, Chile, Argentina, United States, Croatia and France. More than 100 million individuals are chronically exposed to As in drinking water at concentrations above the WHO guideline of $10 \mu g/L$ (Shankar et al., 2014; WHO, 2011). Chronic exposure to As in water has been identified as a risk factor for cutaneous, cardiovascular and endocrine disorders and for certain cancers (Shankar et al., 2014; WHO, 2001). Four recent studies assessed the relation between exposure to As during pregnancy and the occurrence of GDM (Ettinger et al., 2009; Farzan et al., 2016; Peng et al., 2015; Shapiro et al., 2015). The Chinese study of Peng et al. (2015) showed a dose-dependent relation between As concentrations in the meconium and GDM in a population at high levels of exposure. The results of the three other studies, performed in the United States and Canada and involving populations with relatively lower levels of exposure, were discrepant depending on the type of biomarker used and the definition of GDM and on whether the presence of As in drinking water was taken into consideration (Ettinger et al., 2009; Farzan et al., 2016; Shapiro et al., 2015). Only Farzan et al. (2016) assessed the relation between exposure to As in the home tap water and the occurrence of GDM (n = 14) and/or glucose intolerance (n = 105). Exposure to As in home tap water was not statistically associated with the risk of disruption of glucoregulation (GDM or glucose intolerance) (OR = 1.0, 95%CI: 0.9-1.1) but tended to be associated with a higher risk of GDM (OR = 1.1, 95%CI: 1.0–1.2). The observed risk of GDM or glucose intolerance entailed by exposure to As was greater among obese subjects (OR = 1.7, 95% CI: 1.0-2.8) than among overweight women (OR: 1.0, 95%CI: 0.8–1.2) or those with a normal pre-pregnancy body mass index (BMI) (OR: 0.9, 95%CI: 0.8-1.2). However, the statistical power of the study is weakened by the low prevalence of GDM (1.2%) (Farzan et al., 2016). The effect of As in home tap water on the risk of GDM and the potential interaction between exposure and BMI therefore need to be confirmed, particularly when levels of exposure are relatively low (concentrations between 10 and 50 µg As/L).

The main objective of this study was to assess the association between exposure to As in tap water and the risk of GDM in a sample of French women. The secondary objective was to determine if this association was modified by the pre-pregnancy BMI of the women.

2. Methods

2.1. Local context

Owing to its volcanic origins the Auvergne region in France, where our study was conducted, is particularly concerned by the presence of naturally occurring inorganic As (iAs) in its subsurface. Tap water is predominantly obtained from groundwater sources that are in contact with deep geological strata. As a result, there is a natural contamination of water by iAs in Auvergne that, in the absence of extensive treatments for purification of water, could lead to levels greater than those recommended in French guideline for As in the water supply. Decree n°2001-1220 of 20 December 2001 lowered the recommended amount of As in drinking water in France from 50 to 10 μ g/L (République Française, 2001). Since then, management measures such as strengthening of purification treatments of water and disuse of underground water sources highly contaminated by As have been progressively implemented in Auvergne by health authorities. The number of inhabitants supplied with water whose As concentration was higher than

Table 1

Number of inhabitants in Auvergne (France) exposed to arsenic concentrations higher than $10 \mu g/L$ and $50 \mu g/L$ in tap water between 2001 and 2014.

Years	Number of inhabitants in Auvergne region ^a	Number (%) of inhabitants exposed to As in tap water higher than ^b :	
		10 µg As /L	50 µg As /L
2001	1 315,944	137,572 (10.5)	2346 (0.18)
2003	1 323,406	125,008 (9.4)	2313 (0.17)
2006	1 335,938	90,984 (6.8)	370 (0.03)
2010	1 347,387	31,473 (2.3)	(< 0.01) ^c
2014	1 360,637	622 (0.05)	(< 0.01) ^c

^a Reference: French National Institute for Statistics and Economic Studies (INSEE). Estimation of the population by department, sex and age (http://www.insee.fr/fr/themes/detail.asp?reg_id=99&ref_id=estim-pop).

^b References: Data provided by the Health authorities (ARS Auvergne, 2015, 2007).

 $^{\rm c}$ The exact numbers of inhabitants exposed to concentrations higher than 50 $\mu g/L$ are not available. Only percentages are known.

10 μ g/L (and more rarely than 50 μ g/L) steadily decreased, from 140,000 (10.5% of the population) in 2001 to 31,000 (2.3%) in 2010 (Table 1) (ARS Auvergne, 2015, 2007). Hence, up to the year 2010 the Auvergne was an appropriate region in which to assess the effects of exposure to low levels of As (between 10 and 50 μ g/L) on the occurrence of chronic diseases. It was decided to select the three years of 2003, 2006 and 2010 for investigation in our study because for the intermediate years (2004 for example), data on As levels in water may have fluctuated due to implementation of management measures.

2.2. Study design

A semi-ecological study (Künzli and Tager, 1997) was conducted: data concerning exposure to As were aggregate and medical/obstetric data including the diagnosis of GDM were collected retrospectively on an individual basis after childbirth.

2.3. Study participants

The study population was made up of women who gave birth at the Clermont-Ferrand University Hospital in Auvergne. Up to 2009, there were two maternity departments in the hospital, the Polyclinique and the Maternité Hôtel-Dieu. In 2010, the two were merged. Inclusion criteria for our sample were women who had given birth at the Hôtel-Dieu of Clermont-Ferrand between 1 January and 31 December in the years 2003 and 2006 and women who had given birth at the Clermont-Ferrand University Hospital between 1 January and 31 December 2010. Exclusion criteria were women who had given birth at the Polyclinique (because this maternity department did not supply data to the national Association of Users of Computer Records in Paediatrics, Obstetrics and Gynaecology [Audipog] in the years selected for study in this research); medical termination of pregnancy; women not resident in Auvergne at the time of birth and those whose commune of residence at the time of birth was unknown; women who had not been screened for GDM, or only incompletely (glucose challenge test > 1.30 g/L but oral glucose tolerance test (OGTT) not performed); those with no record of screening in their medical file; and women with pre-pregnancy diabetes, either type 1 or type 2. During the three years under study, there were 6332 births in the maternity departments taking part. In all, 5053 women (79.8%) were included in the study (Fig. 1).

2.4. Definition of gestational diabetes mellitus

Before 2010, screening policy for GDM at the Clermont-Ferrand University Hospital was that recommended by the French National College of Gynaecologists and Obstetricians (CNGOF, 1996). Screening was systematic for all women, including those with no known risk Download English Version:

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