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Association between plasma fluoride levels and pregnancy complications in women living in the rural and urban areas of Settat-Morocco

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ABSTRACT

Aims: This study aimed to investigate the relationship between plasma fluoride levels and pregnancy complications among rural and urban women living in the Settat province of Morocco, where fluorosis is endemic.

Methods: This cross-sectional study included pregnant women permanently residing in the province of Settat who visited the Provincial Hospital Hassan II. A close-ended questionnaire was completed to verify the presence or absence of pregnancy complications, including abortion, fetal and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension. In addition, blood was collected from all participants and fluoride levels were determined.

Results: The sample included 511 rural (43.8%) and urban (56.2%) pregnant women with a mean age of 26.9±6.1 years. The prevalence of pregnancy complications was significantly higher in rural pregnant women (abortion=13.2%; fetal and neonatal complications=4.8%; pregnancy induced-hypertension=1.4%) than in urban areas (abortion=6.7%; fetal and neonatal complications=2.2%; pregnancy induced-hypertension=0.9%) ($p<0.05$). Plasma fluoride levels were also significantly higher in rural participants with a means of 0.036±0.009 mg/L than in urban areas with a means of 0.034±0.008 mg/L ($p<0.05$). However, in both rural and urban participants, the results showed that there was no correlation between plasma fluoride levels and abortion ($r=0.068$; $p=0.247$), fetal and neonatal complications ($r=-0.008$; $p=0.890$), diabetes mellitus ($r=-0.018$; $p=0.975$) and pregnancy induced-hypertension ($r=-0.063$; $p=0.285$).

Conclusions: Higher plasma fluoride levels were found in rural pregnant women than in urban ones. However, no significant correlation was found between plasma fluoride levels and the studied pregnancy complications, despite their higher prevalence in rural women.

Introduction

Fluoride is a chemical element belonging to the halogen family. It is widely distributed in the environment mainly in soil, air, and water (1). At the recommended doses, this element plays an essential role in increasing the structural stability of teeth and bones. It is also involved in the growth of both humans and animals (2). However, chronic exposure to high levels of fluoride can lead to chronic intoxication, such as dental and skeletal fluorosis (3). Furthermore, prolonged exposure to this halogen can induce other toxic effects in the reproductive, nervous, and immune systems, leading to non-skeletal fluorosis (4). In many parts of the world, fluorosis is a significant public health concern. It is endemic in more than 20 countries,

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although it is most prevalent in tropical areas, with China and India among the worst-affected nations (5). Other regions, including the Middle East, South America, and Africa (Morocco, Tanzania, South Africa, Kenya, Ghana, and Sudan), are also poisoned (5). Moreover, it was documented that fluoride intake through groundwater is the major contributor to fluorosis and has become one of the most critical issues affecting human health (6). Normally, drinking water is considered contaminated when its fluoride level is between 1.1 and 2.5 ppm and toxic when its fluoride level is greater than 2.5 ppm (7). Hence, the World Health Organization reported that fluoride-rich drinking water exposes many countries to a high risk of being affected by high levels of fluoride (8).

The association between plasma fluoride levels and the prevalence of pregnancy complications is well established in women living in several endemic fluorosis areas (9-11). In these studies, a positive correlation between plasma and urinary fluoride levels and pregnancy complications was reported. In contrast, to the best of our knowledge, no study has focused on pregnancy complications in women living in Moroccan endemic fluorosis areas. In this country, fluorosis is considered a major problem because of its wide distribution (2). There are two types of fluorosis, the first is called hydrotelluric, where the contamination sources are soil and water; it is localized in phosphate areas. The second type is called industrial fluorosis, where the contamination source is air; it is localized in industrial areas (2). Additionally, it was reported that chronic consumption of high fluoride levels through groundwater is the major contributor to fluorosis in humans and several other species (12). Concerning Settat province, where fluorosis is hydrotelluric (13), it includes both urban and rural areas. Increasingly, the rural population consumes well water containing high fluoride levels (14), whereas the urban population consumes tap water that is filtered and controlled. This suggests that rural populations are more exposed to fluoride excess. Therefore, the present study aimed to investigate the relationship between plasma fluoride levels and pregnancy complications among rural and urban women living in the Settat province.

Methods

Study design

The current work was designed as a cross-sectional study that included rural and urban pregnant women aged between 18 and 45 years, who visited the Provincial Hospital Hassan II of Settat province, Morocco in 2019. This province is one of the Moroccan endemic fluorosis areas (14).

The current research was conducted according to the ethical principles of the Helsinki Declaration of the World Medical Association in 1964, amended by the General Assembly of Fortaleza, Brazil, October 2013. The authorization N°1295/18 from the Direction of Epidemiology and Diseases Control of the Ministry of Health of Morocco was obtained before conducting this study.

Inclusion and exclusion criteria

All pregnant women permanently residing in the province of Settat who visited the Provincial Hospital Hassan II during the study period were considered as the source population. After excluding unconfirmed pregnancies and temporary inhabitants in the province, the study sample was formed out of 511 participants.

General and medical information

To collect the general, medical, and obstetrical information of the population study, a close-ended questionnaire was developed and validated in the presence of the research team. Subsequently, it was tested in a similar population to ensure it was understandable. The questionnaire contained open and closed questions and focused on general information such as age, origin, educational level, medical and obstetric information through the verification of the presence or absence of dental stains, and pregnancy complications including abortion, fetal and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension.

Determination of plasma fluoride levels

Blood samples were collected from venous blood using heparin tubes and centrifuged (3000 g for 15 minutes) to obtain plasma samples. Then, one volume of each sample was mixed with the same volume of total ionic strength adjustment buffer (TISAB II). Plasma fluoride levels were measured using a fluoride electrode (Thermo Scientific Orion 96-09, Orion Research, Cambridge, MA, USA) coupled to an analyzer ion (Star A214, Thermo Scientific Orion). The electrode was calibrated with standard fluoride solutions at concentrations of 0.025, 0.050, 0.075, and 0.1 mg/L and prepared with the same reagent used for the samples. Plasma fluoride levels in women without pregnancy complications and those with abortion, fetal and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension were measured and expressed in mg/L.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to evaluate whether the data were normally distributed. The non-normally distributed numeric data were compared using the Mann-Whitney U test, and a p-value of 0.05 was considered statistically significant. The results were summarized as mean±standard deviation (SD), and the categorical data are presented with count (n) and percentage (%) values. We analyzed the correlations between plasma fluoride levels and

each complication in rural and urban women using Pearson's correlation test or Spearman's correlation test.

Results

Descriptive characteristics

The sample included 287/511 (43.8%) rural and 244/511 (56.2%) urban pregnant women with a mean±SD age of 26.9±6.1 years. Based on the questionnaire data, a remarkable variation in educational level was observed between rural and urban participants. Among rural women (n=287), 175 (61.0%), 98 (34.2%), and 7 (2.5%) subjects had primary, secondary, and higher educational levels, respectively. Among urban women (n=224), 70 (31.2%), 138 (61.6%), and 15 (6.7%) subjects had primary, secondary, and higher educational levels, respectively. The remaining 7 (2.5%) rural subjects versus 1 (0.4%) urban subjects were illiterate. Dental stains were significantly more common in rural participants than in urban participants (Table 1). Rural participants also showed poorer oral hygiene (Table 1). Regarding plasma fluoride levels, rural pregnant women had significantly higher plasma fluoride levels (0.036±0.009 mg/L) than their urban counterparts (0.034±0.008 mg/L) ($p<0.05$) (Table 1).

Prevalence of pregnancy complications

Regarding pregnancy complications, 79.8% of rural versus 88.9% of urban participants did not report any pregnancy complications (Table 2). Abortion and fetal and neonatal complications were significantly higher in rural pregnant women than in urban subjects ($p<0.05$). The prevalence of diabetes mellitus and pregnancy-induced hypertensive complications was not significantly different between rural and urban participants ($p>0.05$) (Table 2).

Relationship between plasma fluoride levels and pregnancy complications

In both rural and urban participants, plasma fluoride levels were significantly ($p<0.05$) higher in women with abortion, fetal and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension than in those without these complications. When rural and urban women who reported the same complications were compared, we found significantly higher plasma fluoride levels only in pregnant women from rural areas with fetal and neonatal complications compared with those from urban areas ($p<0.05$). However, no significant difference was observed between rural and urban participants with abortion, diabetes mellitus, and pregnancy-induced hypertension ($p>0.05$) (Table 3). Additionally, in both rural and urban participants, the

Table 1. Dental stains, oral hygiene and plasma fluoride in rural and urban participants

Origin	Rural (n=287)	Urban (n=224)	p-value
Dental stains, n (%)	188 (65.5)	33 (14.7)	**0.001**
Poor oral hygiene, n (%)	181 (63.1)	69 (30.9)	**0.001**
Plasma fluoride (mg/L), mean±SD	0.036±0.009	0.034±0.008	**0.018**

The results are significant at the level of 0.05.
SD: Standard deviation

Table 2. Prevalence of studied pregnancy complications in rural and urban pregnant women

	Rural (n=287)	Urban (n=224)	p-value
Without complication, n (%)	229 (79.8)	199 (88.9)	**0.006**
Abortion, n (%)	38 (13.2)	15 (6.7)	**0.016**
Fetal and neonatal complications, n (%)	14 (4.8)	5 (2.2)	**0.047**
Diabetes mellitus, n (%)	2 (0.7)	3 (1.3)	0.146
Pregnancy induced-hypertension, n (%)	4 (1.4)	2 (0.9)	0.247

The results are significant at the level of 0.05

Table 3. Plasma fluoride levels in rural and urban participants according to their pregnancy complications

Origin	Rural (n=287)	Urban (n=224)	p-value
Without complication (mg/L), mean±SD	0.036±0.009	0.034±0.008	**0.005**
Abortion (mg/L), mean±SD	0.038±0.011	0.039±0.011	0.425
Fetal and neonatal complications (mg/L), mean±SD	0.038±0.003	0.035±0.008	**0.018**
Diabetes mellitus (mg/L), mean±SD	0.039±0.001	0.039±0.011	0.413
Pregnancy induced-hypertension (mg/L), mean±SD	0.041±0.001	0.039±0.004	0.125

The results are significant at the level of 0.05.
SD: Standard deviation

results showed that there was no correlation between plasma fluoride levels and abortion (r=0.068; p=0.247), fetal and neonatal complications (r=-0.008; p=0.890), diabetes mellitus (r=-0.018; p=0.975) and pregnancy induced-hypertension (r=-0.063; p=0.285) (Table 4).

Discussion

In Morocco, fluorosis extends to all phosphate areas (2,13). In these endemic areas, it has been reported that the weathering of phosphate rocks releases a large amount of fluoride, which contaminates groundwater and soil (2), causing hydrotelluric fluorosis (13). For instance, in Settat province (Morocco), a study revealed a high fluoride level in well water (14). Consequently, direct consumption of this contaminated water and/or the consumption of natural products (cereals, fruits, etc.) that grow in the contaminated soil leads to various toxic effects (15). After its intake, fluoride can lead to several adverse effects in different forms of fluorosis in humans (12,16). Recent studies have shown that fluoride can increase pregnancy complication risks (6,17). Conversely, low levels of awareness and prevailing dietary and behavioral practices may put populations at risk of high fluoride intake (18).

In the current study, it was revealed that the educational level was lower in rural participants than in those from urban areas. These results could be explained by family income and denial by the parents as these could be the most common reasons for school dropout in rural areas (19). Additionally, our findings showed that rural pregnant women had poorer oral hygiene than their urban counterparts. This may explain the higher prevalence of dental stains observed among rural participants. In this context, an association between oral health and several socioeconomic factors such as poverty, education, and health disparities between urban and rural areas has been documented previously (20).

Concerning the prevalence of pregnancy complications in both studied areas, abortion and fetal and neonatal complications were higher in rural pregnant women than in urban ones. In this sense, a previous study conducted in the province of British Columbia (Canada) reported that rural pregnant women had higher rates of severe maternal and neonatal morbidity (21). Another study conducted in Ethiopia found that rural women were more likely to experience adverse pregnancy outcomes, including abortion and neonatal deaths, compared with their urban counterparts (22). Given that blood is the main transporter of fluoride in the body, plasma fluoride level is an essential parameter for diagnosing the chronic toxic effects of fluoride, mainly in pregnant women (23,24). In this study, plasma fluoride concentration in pregnant women showed that its average was significantly higher in rural pregnant women compared with those of urban origin. This finding could be explained by the drinking water sources in each area, as the rural population consumes well water, which is contaminated by fluoride excess in phosphate rocks, whereas the urban population consumes tap water, which is filtered and controlled. Similarly, another study conducted in India revealed a positive correlation between plasma fluoride in pregnant women and fluoride in groundwater (25). To compare the values obtained in this study, it was revealed that they were lower than those obtained in pregnant Polish women (26) and higher than those obtained in Mexican pregnant women (27) and American pregnant women living in northern California (24). The current study contributes to the existing literature by providing new information on plasma fluoride concentrations in pregnant women in Morocco and highlighting the potential factors that may influence these concentrations.

Previous studies have investigated the passage of fluoride across the placenta during pregnancy (6,28). Exposure to a high fluoride level during this critical physiological stage can cause several pregnancy complications (6). These may be related to the high fluoride concentration, as reported in an Iranian study (29). In the present study, among both rural and urban participants, plasma fluoride levels were significantly higher in women with abortion, fetal and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension than in those without these complications. This is in agreement with other studies that reported that fluoride consumption increased the risk of anemia (6), abortion (29), low birth weight, preterm delivery, and poor APGAR count (9,11,30). This suggests that there is a link between fluoride consumption and certain adverse pregnancy outcomes. For pregnant women, it is necessary to consider this potential risk factor when making decisions about prenatal care and fluoride intake. The finding that there was no correlation between plasma fluoride levels and abortion, fetal

Table 4. Correlation analysis of plasma fluoride levels with abortion, fetal and neonatal complications, diabetes and pregnancy induced-hypertension in rural and urban women

	Rural		Urban	
Parameter	r value	p-value	r value	p-value
Without complication	-0.038	0.515	0.042	0.525
Abortion	0.068	0.247	-0.060	0.371
Fetal and neonatal complications	-0.008	0.890	-0.012	0.854
Diabetes	0.0018	0.975	0.066	0.323
Pregnancy induced-hypertension	-0.063	0.285	-0.059	0.379

and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension in both rural and urban participants may be attributed to several factors. First, because of the reduced number of participants in this study cohort studies on a large population are recommended to obtain clearer results. On the other hand, factors other than fluoride exposure could influence the prevalence of pregnancy complications. It was documented previously that genetics, immunological, and infectious factors could lead to abortion in women (31). Another study showed that maternal age, placental abruption, and pre-existing maternal pathologies (obesity, diabetes mellitus, hypertension) increased the risk of intrauterine fetal death (32). Furthermore, it was reported that maternal lifestyle factors such as obesity, physical activity, medication, poor nutrition, and coffee consumption are also associated with pregnancy complications (33,34). In summary, consistent with the literature, differences in plasma fluoride levels were found between rural and urban pregnant women.

Study Limitations

This study represents the first of its kind to be conducted in Morocco, focusing on the important topic of maternal and fetal health, which is a global priority. However, this study has several limitations. Most importantly, the sample size was small. Additionally, some information was unavailable due to incomplete or outdated health records. Finally, the results were not adjusted for potential covariates of fluoride intake.

Conclusion

In conclusion, this study showed that plasma fluoride levels were higher in rural pregnant women than in those from urban areas. However, despite the higher prevalence of abortion, fetal and neonatal complications, diabetes mellitus, and pregnancy-induced hypertension in women of rural origin, there was no correlation between plasma fluoride levels and pregnancy complications. Therefore, further studies in a large population are recommended to obtain clearer results.

Acknowledgments

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Ethics

Ethics Committee Approval: The study was approved by the Hassan First University of Settat, Faculty of Sciences and Techniques of Ethics Committee. The authorization N°1295/18 from the Direction of Epidemiology and Diseases Control of the Ministry of Health of Morocco was obtained before conducting this study.

Informed Consent: Consent form was filled out by all participants.

Authorship Contributions

Concept: A.E., Design: A.E., Data Collection or Processing: L.A.K.M., Analysis or Interpretation: F.H., Literature Search: L.A.K.M., A.R., Writing: L.A.K.M., A.R., B.El.A., B.N.

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