

## Pregnant women living in areas of endemic fluorosis in Senegal and low birth weight newborns: Case–control study

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### Abstract

**Background.** – In developing countries, maternal and neonatal mortality is high. Among the causes of death during the neonatal period, low birth weight is crucial. A dose of fluoride beyond 2 mg/L causes enamel damage, possibly affecting the foetus. The aim of this study was to search for an association between dental fluorosis in the mother and low birth weight of the newborn.

**Methodology.** – This was a case–control study performed in an endemic area in Senegal (Diourbel). It included 108 mothers who gave birth to newborns weighing less than 2500 g (cases) and 216 mothers with newborns weighing greater or equal to 2500 g (controls). Data on sociodemographic, lifestyle, history and pregnancy variables were collected. Those related to water consumption during pregnancy and dental fluorosis (Dean's index) were measured. The data were analyzed by R software. Logistic regression was used to identify associations and the statistical significance level was set to 0.05.

**Results.** – The proportions of mothers consuming well water were 62% among cases versus 43.5% among controls. The score 4 of Dean's Index was reported for 25.9% of cases versus 6.9% of controls. The water consumed and the modal score of Dean's Index were significantly associated with the occurrence of low birth weight adjusted for gender, consanguinity, anemia and hypertension.

**Conclusion.** – Low birth weight was associated with pregnant women living in endemic areas. Defluoridation programs and access for pregnant women and children to high quality water are necessary in areas of endemic fluorosis. # 2012 Published by Elsevier Masson SAS.

**Keywords:** Dental fluorosis; Low birth weight; Endemic area; Senegal; Pregnant women

### 1. Introduction

In developing countries, maternal and neonatal mortality rates remain high [1]. Amongst mortality causes during the neonatal period, low birth weight is decisive. It has been defined by the World Health Organization as a birth weight under 2500 g.

According to the EDS III survey (Health and Demographic Survey) [2] in Senegal, 13.5% of women on average give birth to newborn infants weighing less than 2500 g. These newborn babies are a daily concern due to the difficulties related to their care and the frequent negative impact of low weight on their growth. The high burden of infectious and/or inflammatory disease is amongst the most determinant causes of death. To that we can add dental pathologies, enamel defects, congenital or acquired [3]. Just like other chemicals, fluorine and fluorides have both beneficial and toxic effects with significant implications on public health. Even though we have noted that an optimal dose of 1 mg of fluoride per litre in drinking water is beneficial for the prevention of tooth decay, extended exposure to higher concentrations can lead to adverse effects on enamel and bones [4,5]. In fact, a concentration of fluoride higher than 2 mg/l causes enamel deterioration increasing with fluoride intake, and this can occur in conjunction with other conditions or might increase certain risks. In pregnant women, placental transport of fluorides happens as early as the 19th week of pregnancy [6–9]. In some countries, and more specifically in the United States, several studies have focused on dental fluorosis and low birth weight [3,10,11].

One of the pretexts used to justify water fluoridation is a high prevalence of low birth weight. But fluoridation is beneficial only for newborn infants whose birth weight is greater than or equal to 3400 g [12]. These studies focused on the increase of the prevalence of dental fluorosis due to the fact that a significant proportion of newborns have a low birth weight (under 2500 g).

However, we have not seen any study looking at the potential links between dental fluorosis in the mother, exposure to fluorides and low birth weight in infants as an impact. For that reason, we wish to test the assumption that there is a risk of giving birth to a low weight infant in mothers drinking high fluoride water who are affected by dental fluorosis, especially in endemic areas. The objective is to consider a potential link between dental fluorosis, fluoridated water intake by mothers and birth weight among infants.

## **2. Methodology**

The Diourbel region covers a surface area of 4359 km<sup>2</sup> with a population of 1,049,954 inhabitants. This area has endemic dental fluorosis with concentrations of 4.7 and 0.009 mg/L for drill water and well water respectively [13]. The maternity ward of Diourbel's Heinrich Lubcke Hospital delivers an average of 180-250 babies per month. The morbidity-mortality rate is 24 per thousand. This maternity ward constituted our study environment.

This was a case-control study conducted at the Diourbel regional hospital concerning all newborn infants and parturient mothers giving birth at the Heinrich Lubcke Hospital.

### **2.1. Population inclusion criteria and definition**

Cases considered in this study are mothers giving birth in this institution to a newborn infant whose weight is under 2500 g. Controls are mothers of a newborn infant whose weight is greater than or equal to 2500 g. In order to be included, parturient mothers must hold a pre-natal Medical Attendance Record.

### **2.2. Non-inclusion criteria**

Cases excluded from this study are mothers with a gynecologic infection during pregnancy, mothers giving birth to a stillborn baby and mothers giving birth to twins. Mothers giving birth at home and who later came to this institution in order to get secondary treatment and mothers whose health condition prevents a clinical oral examination have also been excluded.

Cases have been recruited successively in order of arrival. As far as controls are concerned, they were randomly selected among the population of parturient mothers in the maternity ward. Newborn infants were matched according to gender (whenever a case is male, the next two controls were also male).

### **2.3. Sample size**

The sample size was calculated using the Epi 2000 software. Considering a risk of 5% with a power of 80%, we selected a theoretical exposure of 35% among the control cases in view of the strong prevalence of dental fluorosis in Diourbel. The risk of giving birth to a low weight infant has been set at 2 when the mother has a moderate dental fluorosis score. Thus, the sample was made up of 218 controls versus 109 cases, i.e. two controls for every case.

### **2.4. Data collection**

Before asking mothers to fill in the questionnaires, we instructed them about the objectives and importance of this study. For ethical reasons, we also asked them to provide consent, and in order to motivate them, a training session on hygiene has also been proposed subsequent to the survey. Data were collected using a pre-tested questionnaire among a group of ten patients at the Diourbel maternity ward. Data collection was done every day and involved all patients that came to the hospital's maternity ward and complied with the selection criteria. This happened between February and May 2010.

Collected data includes:

- Sociodemographic characteristics: age, occupation, income, weight, height, Body Mass Index (BMI=weight/height<sup>2</sup>), consanguinity, number of weeks of amenorrhea (SA), parity, low weight
- Lifestyle: smoking, coffee intake, tea intake;
- General history: anemia, hypertension, diabetes, malaria, pre-eclampsia;
- Fluorosis data: water intake, Dean's score.

Twenty four hours after delivery, mothers underwent a maintenance treatment followed by a clinical dental examination.

## 2.5. Measuring the exposure

This is related to independent variables: sociodemographic variables, history, and the two main independent variables, i.e. dental fluorosis and water intake during pregnancy. All of the natural teeth present in the mouth were taken into account during the clinical examination.

Assessment of severity of the condition was provided by the Dean's index [14]. This epidemiological index of interest has been developed in order to diagnose the severity of a tooth's condition using a numerical and sequential score. Measurements were performed by a trained dentist using a complete tray during a standardized dental examination.

## 2.6. Measuring the outcome

The measurement of the outcome (babies' weight) was done using a baby scale. The scale is a 2008 Kern MBE 10K10 version 1.0, acquired for our needs. Measurements were performed by a midwife trained in pelvic ultrasound exams and in the use of this type of scale.

## 2.7. Data analysis strategy

Data entry was carried out using the Epi 2000 5.3.1 software. Univariate analysis of ratios, averages and their standard deviations was also performed with this software. Regarding the "dental fluorosis" variable, Dean's scores were considered without any change. The dependent variable « low weight » was coded as 1 when the newborn's weight was under 2500 g and as 0 when it was higher or equal to 2500 g.

Associations between qualitative variables were analyzed using the Chi<sup>2</sup> test or one of its variations (Yates and Fisher) and their strengths were determined by ratios of scores and their confidence level. The modelling used a backward selection procedure which was developed using the variables associated with a low birth weight with a "p" value lower than 0.20 in a univariate analysis. At each step, the variable associated with the higher "p" value was eliminated from this model at a threshold value of 5%. The procedure stopped whenever all remaining variables in the model reached a "p" value lower than the threshold value, with the exception of those that are forced (dental fluorosis, water intake and parity). In order to monitor confusion, every time a variable exits, the score ratio variation of the main "Dean's index" independent variable was checked by calculating the relative variation. Interactions with the index were tested. The R software version 2.9.0 is used in the multivariate analysis. Results were considered marginally significant at  $5\% \leq p \leq 7\%$  and significant when p was lower than 5%.

## 3. Results

Within the subsample of mothers that had one infant of low birth weight, only one did not undergo a clinical dental exam due to health reasons; and two among the control group, for the same reasons. These mothers were excluded from this study, and in the end the analysis deals with 108 cases versus 216 controls.

### 3.1. Description of sociodemographic characteristics, lifestyles, medical history

Table 1 shows that the variables parity, consanguinity, anemia, hypertension and pre-eclampsia are significantly associated with low weight using a univariate analysis. Malaria was marginally associated with low weight.

**Table 1**  
Description of mother cases and controls.

Variables	Cases (108)	Controls (216)	
<b>Sociodemographic characteristics</b>			
	Average (ET)	Average (ET)	p-value
Age (years)	27 (6.06)	27.68 (6)	0.34
Weight (kg)	60.48 (8.10)	62.16 (8.79)	0.09
Height (cm)	166.94 (5.8)	166.52 (8.75)	0.65
Body mass index (kg/m <sup>2</sup> )	21.66 (2.4)	22.98 (11.19)	0.22
Parity in unit	3.05 (1.88)	3.6 (1.9)	0.014
Income $\geq$ 100 000 en CFA francs (%) <sup>a</sup>	48.1	46.8	0.81
Consanguinity(%)	48.1	28.7	0.0005
<b>Lifestyle related characteristics</b>			
	%	%	
Active smoking	1.9	0.5	0.53
Passive smoking	32.4	24.1	0.11
Coffee	75.0	73.1	0.72
Tea	72.2	74.1	0.72
<b>Medical history</b>			
	%	%	
Anemia	24.1	9.3	0.0003
Diabetes	6.5	3.7	0.26
Hypertension	23.1	11.6	0.007
Malaria	17.6	10.2	0.06
<b>Birth outcome characteristics</b>			
	%	%	
Vaginal delivery	99.1	99.1	0.54
Pre-eclampsia	23.1	11.6	0.007
Number of weeks of amenorrhea (SA)	39.05		
<sup>a</sup> 655,957=1 €	(1.02)	39.17 (1.2)	0.3

**Table 2**  
Score ratios for fluorosis scores and type of water intake among mothers, simple logistic regression.

Variables	Modalities	Cases		Controls		p-value
		n=108 (%)	n=216 (%)	RC	IC	
Water intake	Mineral	11 (10.2)	30 (13.9)	1	–	
	Well	30 (27.8)	92 (42.6)	0.89	[0.39–1.98]	0.77
	Drilling	67 (62)	94 (43.5)	1.94	[0.91–4.15]	0.07
Index (score)	0	7 (6.5)	13 (6)	–	–	–
	1	23 (21.3)	113 (52.3)	0.38	[0.14–1.05]	0.062
	2	26 (24.1)	61 (28.2)	0.79	[0.28–2.21]	0.656
	3	24 (22.2)	14 (6.5)	3.18	[1.03–9.86]	0.044
	4	28 (26)	15 (6.9)	3.47	[1.14–10.55]	0.029

The overall p-value of the index is  $< 0.0001$  and 0.045 for water ingested during pregnancy.

### 3.2. Description of variables related to fluorosis

Table 2 shows the associations between the type of water intake during pregnancy, Dean's index and low birth weight using a simple logistic regression. The tested interactions (tea index and SA index) are not significant ( $p=0,914$  and  $p=0,938$  respectively).

### 3.3. Factors associated with low birth weight after adjustment

Table 3 shows the final model selected after a multivariate analysis using a top-down manual procedure. We find that the risk of giving birth to a low weight infant

**Tableau 3**

Score ratios for characteristics associated to low birth weight, using a top-down manual regression.

Variables	RC	IC	p
<b>Ingested water</b>			
Mineral water	1	1	0,04
Well water	0.88	[0.5–2.51]	
Drill water	1.99	[1.3–3.67]	
<b>Dean's index</b>			
0	1	–	
1	0.31	[0.11–0.91]	< 0,001
2	0.66	[0.23–1.96]	
3	2.77	[0.85–9.02]	
4	3.2	[1.1–9.43]	
<b>Parity</b>			
Unit	1,2	[1.03–1.39]	0.017
<b>Consanguinity</b>			
No	1	[1.18–3.55]	0.011
Yes	2.04		
<b>Anemia</b>			
No	1	[1.78–7.72]	< 0.01
Yes	3.7		
<b>Hypertension</b>			
No	1	[1.35–5.61]	0.005
Yes	2.75		

is 2.77 higher among mothers when the score is equal to 3; it goes up to 3.2 when the score is equal to 4 after adjusting for parity, consanguinity, anemia and hypertension.

## 4. Discussion

This work has allowed us to study the association between low birth weight and dental fluorosis. The risk associated with drill water intake is 1.99 [1.3– 3.67], whereas the risk associated with the most severe Dean's index score is 3.2 [1.1–9.43] after adjusting for parity, consanguinity, anemia and hypertension.

### 4.1. Limit and methodological considerations

We have used the Epi info software in order to determine the sample size while taking into account a theoretical exposure to fluorosis of 35% among controls due to the endemic nature of fluorosis in the area. This procedure could overestimate the disease, especially as it is possible that some mothers were not born in an endemic area or have not lived during a risky period within an endemic area. There might also be a difference in the quality of drinking water used by

mothers, and this would potentially modify the link between exposure and results. However, the ratio of one case versus two controls and the random selection of subjects help to minimize bias. In order to lessen the residual confusion, we have adjusted several sociodemographic factors, lifestyles or medical histories. During data collection, one single person took the exposure measurement and in a totally blind manner. As for the outcome, it was recorded by the midwife. This process has allowed us to minimize the non differential classification bias.

#### 4.2. Sociodemographic characteristics

Several studies have previously integrated sociodemographic factors into the study of low birth weight outcomes. The mother's age, in particular in the case of early pregnancies, can influence intrauterine foetal growth [15]. However, age is not linked with low weight in the endemic fluorosis area. In their study about low weight and periodontal disease, Khader et al. [16] found a link between age and low weight.

The Body Mass Index, used to assess risks related to overweight in adults, is not found to be related to low weight, even before adjustment. The case control study conducted by Ndiaye et al. in 2006 [1] in Senegal has also not demonstrated a link between Body Mass Index and low weight.

Parity was significantly associated with low birth weight after adjusting for the Dean's index, consanguinity and hypertension, and the retrospective study of Bobossi–Serengbe [17] in Central Africa showed similar results.

A couple's monthly income greater than or equal to 100 000 CFA francs, ie. 152,4 €, is not often found, especially among cases, and this can be explained by the living conditions prevailing in the interior of the country where promiscuity and poverty are relatively frequent. Contrary to Camara et al. [18], our results have not shown a link between income and low birth weight. These disparities would be rather due to the difficulty of finding a reliable indicator in order to measure the income level of populations. Pitiphat et al. [19] in 2008 in the United States, among a cohort of 1635 women, have also noted the absence of a link between income and pregnancy outcome.

In this study, it has not been an easy task to determine the level of consanguinity using a family tree. Yet, our study shows that within a context of endemic fluorosis, the risk of giving birth to a low weight infant is 2.04 times higher in the case of a consanguine union. Wharton [20] reported a frequency of 17% of hypotrophic babies born of a marriage between first cousins in a Pakistani population.

#### 4.3. Mothers' lifestyle

The direct consumption of tobacco (active smoking) in industrialized nations is still a public health problem. It is a risk factor which plays a role in several pathologies [21,22]. In Africa, tobacco is used mostly by men, and then secondary smoke harms their wife's health (passive smoking). However, in our study, we have not found any link between low weight and smoking patterns, and these results are similar to those of Ndiaye et al. [1].

Tea consumption is more important among cases, but this association is not found to be significant in a univariate analysis. Bicalho and Barros [23], in a case-control study involving 354 newborn infants under 2500 g and 354 infants over 3000 g, have not found a link between regular tea consumption and the occurrence of growth delays. The results have also been replicated by Santos et al. in 1998 [24]. Several animal experimental studies have shown the negative effect of catechins found in tea on the absorption of certain proteins and iron in the digestive tract, potentially leading to nutritional deficiencies [23,25]. Thus, if tea had a deleterious impact on foetal growth during pregnancy, it could be explained by the nutritional status.

#### 4.4. Medical history

Anemia is a possible condition during pregnancy, and it is significantly associated with low birth weight in our work. On the other hand, diabetes and malaria are not. Gestational diabetes seems to concern 1 to 4% of pregnancies across the world [26]. However, maternal diabetes can be

complicated by pregnancy-related hypertension leading to placental ischemia, and then leading to a low nutrient and oxygen supply. This might create a condition of chronic foetal distress with an intrauterine growth delay. The link between hypertension and low birth weight has been found to be marginally significant after adjustment for the other variables (2.75; [1.35–5.61]).

#### 4.5. Parameters related to dental fluorosis

Dental fluorosis is a health condition which is endemic across several regions around the world, especially where the soil contains large amounts of fluorine. In our study area, the highest fluoride concentrations have been found in drill water, followed by well water, and we have found that drill water intake is more frequent among cases. After adjusting the Dean's index and other factors, the risk of fluorosis outcome is 1.99 times higher when a mother drinks drill water. The condition of the teeth or the severity of dental fluorosis of parturient mothers is assessed using Dean's index [14]. Using a qualitative interpretation of this index, it becomes apparent that dental fluorosis is clearly more important among case mothers, and that number would increase in proportion to scores. The proportion of women with a score of 3 is also higher among cases than among controls (22% versus 6%). The proportion of women with a score of 4, i.e. obvious fluorosis with opacification and wear pattern of teeth, is of 26% among cases versus 7% among controls.

Comparable results have also been found by Hall [27], indicating that premature infants are more frequently affected by enamel anomalies or defects when compared with infants born at term.

The Dean's index is also significantly linked to low weight if we use a univariate analysis and adjust for parity, anemia, consanguinity and hypertension. The interactions between the index and tea consumption or SA number are not significant. However, using a univariate analysis, the risk of low weight outcomes increases with the score. It is 2.77 times higher among case mothers when the score is equal to 3. And the risk goes to 3.2 when the score is equal to 4, after adjusting for other variables. Bhat and Nelson [28], in a review about enamel defects developed in deciduous dentition, concluded that there is a link between low birth weight and dental fluorosis. Seow [29] also found the same results. However, other researchers in the United States and Norway have not found an association between dental fluorosis and low birth weight [9,10].

While taking into account numerous confounding factors, our results support the hypothesis that within an endemic area, dental fluorosis in pregnant women is associated with a risk of giving birth to a low birth weight infant. These results need further confirmation by other studies.

#### Declaration of interests

Herein the authors declare that they had no conflict of interest at the time of drafting this paper.

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