Antepartum Dental Radiography and Infant Low Birth Weight

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Context Both high- and low-dose radiation exposures in women have been associated with low-birth-weight offspring. It is unclear if radiation affects the hypothalamus-pituitary-thyroid axis and thereby indirectly birth weight, or if the radiation directly affects the reproductive organs.

Objective To investigate whether antepartum dental radiography is associated with low-birth-weight offspring.

Design A population-based case-control study.

Participants and Setting Enrollees of a dental insurance plan with live singleton births in Washington State between January 1993 and December 2000. Cases were 1117 women with low-birth-weight infants (<2500 g), of whom 336 were term low-birth-weight infants (1501-2499 g and gestation ≥37 weeks). Four control pregnancies resulting in normal-birth-weight infants (≥2500 g) were randomly selected for each case (n=4468).

Main Outcome Measures Odds of low birth weight and term low birth weight by dental radiographic dose during gestation.

Results An exposure higher than 0.4 milligray (mGy) during gestation occurred in 21 (1.9%) mothers of low-birth-weight infants and, when compared with women who had no known dental radiography, was associated with an adjusted odds ratio (OR) for a low-birth-weight infant of 2.27 (95% confidence interval [CI], 1.11-4.66, P = .03). Exposure higher than 0.4 mGy occurred in 10 (3%) term low-birth-weight pregnancies and was associated with an adjusted OR for a term low-birth-weight infant of 3.61 (95% CI, 1.46-8.92, P = .005).

Conclusion Dental radiography during pregnancy is associated with low birth weight, specifically with term low birth weight.


METHODS

Identification of Cases and Controls

We conducted a population-based case-control study linking dental utilization data from Washington Dental Service (WDS), a not-for-profit dental insurance company, and vital record birth certificates from Washington State. All women between the ages of 12 and 45 years, with a dental treatment between January 1, 1993, and December 31, 2000, were identified, and a client file was created that contained the first and last name, address, city, zip code, and birth date. This file was sent to the birth certificate data manager (with no affiliation to WDS) who created a unique identifier for each record and linked the data to the vital records.

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record birth certificates using both deterministic and probabilistic matching procedures. Only singleton births were included.

The combination of the mother’s exact birth date along with the mother’s first name and either the father’s last name or mother’s maiden name gave a conclusive match for 94.1% of the matched sample of women. Exact date of mother’s birth, along with a partial name match (first 5 characters of last name and first character of first name) accounted for a further 2.7% of matches. Partial name matches (first 7 characters of last name and first 5 characters of first name) and either an address match (0.5%) or transposed date of mother’s birth year, month, or day segment (2.7%) accounted for the remaining matches.

During this matching process, the WDS data manager only received infant birth dates from the birth certificate data manager, and the birth certificate data manager did not receive dental utilization data from WDS. All successful matches combined with infant birth dates (n=29,215) were sent back to WDS where it was determined whether eligibility for dental services existed during a period 40 weeks prior to birth and for how many months eligibility existed. Prior to 1995, eligibility for dental services could only be determined for those women who had at least 1 dental visit, whereas subsequent to 1995, eligibility could be determined regardless of whether a dental visit occurred. This change in method of determining eligibility did not affect the reported findings.

The unique identifiers of those women eligible for dental services during pregnancy were sent to the birth certificate data manager who then selected the case-control study population. The case group consisted of all pregnancies resulting in LBW infants. Four normal-birth-weight (NBW) infants (2500 g-5414 g) were randomly selected for each case without matching. Each NBW infant had an associated random number, which was generated using the “ranuni” function in SAS, version 8.2 (SAS Institute Inc, Cary, NC). The 4468 infants with the lowest random numbers were included in the sample. Both the WDS and birth certificate data managers subsequently stripped their respective data files of personal identifiers and sent them to the University of Washington where linking occurred using the patient unique identifier. Human subject approval was obtained from the Human Research Review Board of the Department of Health in the State of Washington.

Low birth weight was defined as any infant weighing less than 2500 g. Low-birth-weight infants were subdivided into 3 categories: very low-birth-weight (VLBW) infants (≤1500 g), preterm low-birth-weight (PLBW) infants (between 1501-2499 g and <37 weeks’ gestation), and term low-birth-weight (TLBW) infants (1501-2499 g and ≥37 weeks’ gestation). Sixteen infants with a birth weight between 1501 and 2499 g and of unknown gestational age could not be classified.

**Dental Radiography Doses**

Dental radiography can affect at least 3 organs in the head-and-neck region that are potentially involved in pregnancy outcomes: the hypothalamus, the pituitary, and the thyroid. Because of the evidence on thyroid susceptibility to radiation, and because of the existing hypothesis that radiation-induced thyroid dysfunction causes LBW, radiation doses to the thyroid were calculated. For each woman, the date and type of each dental radiograph taken was abstracted from the dental utilization data, doses were assigned to each type of radiographic exposure, and summed. Doses were estimated based on a nationwide 1993 dental survey evaluation of x-ray trends and published thyroid radiation doses. Given that mean skin exposure of a dental radiograph is typically 2.17 milligray (mGy), that 90% of the sampled dental offices use D-speed film, and that the mean kilovoltage in dental offices is approximately 70, a full-mouth dental survey consisting of 21 radiographs is expected to result in a typical dose to the thyroid of an adult female of 1.6 mGy. The dose to the thyroid of a periapical dental radiograph, while dependent on the positioning of the x-ray unit, will on average equal 0.08 mGy. In a female patient, 4 bitewings is 14% of the total radiation dose of a full-mouth radiograph or 0.22 mGy. A cephalometric radiograph was estimated as delivering a dose of 0.46 mGy to the thyroid and 0.12 mGy. Both are estimates to the central thyroid region. Doses to the left and right lobe of the thyroid can be substantially higher. We did not have information on thyroid shield use, but its use for intraoral films is reported to be low (Mike Odlaug, MPH, written communication, December 2003). The calculated cumulative radiation doses during gestation were categorized into 3 dose groups: 0 mGy (no known dental radiography), 0.1-0.4 mGy, and higher than 0.4 mGy. The value of 0.4 mGy corresponded to the 90th percentile of cumulative radiation doses among women with at least 1 dental x-ray. Radiation doses were also modeled as a continuous variable.

The WDS electronic database is validated both at treatment planning and completion phases by conducting random or data-driven patient record audits. In addition, a recently concluded validation study indicated that the proportion agreement between chart audits and electronic records averaged almost 97% for all dental procedures and 93% for radiographic dental procedures. For all analyses, the radiation dose since the last menstural period prior to pregnancy was calculated. For 109 women (1.9%), the gestational length was not recorded, and an estimate of 40 weeks of gestational length was used. Sensitivity analyses indicated that the inclusion or exclusion of these 109 women did not affect the findings.

**Confounding Variables**

Both the birth certificate records and the dental utilization data provided information on the following variables: maternal age at the time of delivery (cat-
published diabetes, the Kessner Adequacy
the presence of gestational or estab-
puts, parity (categorized into 0, 1-2, and
procedures during pregnancy, marital sta-
quency during pregnancy, dental proce-
duration of eligibility for dental insur-
duress.
procedures, and orthodontic proce-
dures including implants, oral surgery
cedures (eg, periodontal scaling or peri-
cedures (eg, fillings), periodontal pro-
cedures (eg, dental prophylaxis), restorative pro-
agnostic procedures (eg, radiographs,
and nomenclature that is used by WDS
developed a code on dental procedures
ers. The American Dental Association
raphy were also considered as confound-
chronic hypertension.
ning pregnancy, preeclampsia, and
consumption of 1 or more alcoholic
duress.
Dental procedures other than radiog-
raphy were also considered as confound-
ers. The American Dental Association
developed a code on dental procedures and nomenclature that is used by WDS
classes dental procedures into di-
gnostic procedures (eg, radiographs,
examinations), preventive procedures
(e.g, dental prophylaxis), restorative pro-
ces (eg, fillings), periodontal pro-
cedures (eg, periodontal scaling or peri-
dontal maintenance procedures),
endodontic procedures (eg, root canal
fillings), removable prosthetic pro-
cedures, fixed prosthodontic pro-
dclusions including implants, oral surgery pro-
ces, and orthodontic proce-
s.

Statistical Analysis
Between 1993 and 2000, the 5719
women in the selected study sample had
1 singleton birth, 197 women had 2
singleton births, and 4 women had 3
singleton births. To take into account
that the pregnancy outcomes for
women with more than 1 birth are cor-
related events, generalized estimating
equation models were used. Odds ra-
tios (ORs) were calculated using gen-
eralized linear models with an ex-
changeable correlation structure, a logit
link, and a binomial error distribu-
tion. Case-control differences in po-
tential confounders were estimated us-
ing exchangeable correlation matrices,
with the exception of prepregnancy
weight where an independence corre-
lation structure was used. Correlation coef-
ficients and the respective P values
describing the association be-
tween dental radiation and potential
confounders were estimated ignoring
within-subject correlation. The statis-
tical significance level was set at .05.
The impact of missing values was as-
essed with multiple imputations of
missing values using a sequential re-
gression imputation method (Imputa-
tional and Variance Estimation soft-
ware [IVEware], version 2.0, University
of Michigan, Ann Arbor). This method
imputed values for each woman con-
tioned on the other values observed
for that woman. The imputations were
drawn from the posterior distribution
specified by a regression model with a
noninformative prior distribution. Val-
ues were imputed cyclically, each time
overwriting previously drawn values.
Subsequently, regression models were
built using the jackknife repeated rep-
lication technique.

RESULTS
There were 1117 LBW infants born to
women with WDS insurance between
1993 and 2000: 193 VLBW infants, 572
PLBW infants, 336 TLBW infants, and
16 of unknown gestational age
(TABLE 1). A total of 4468 NBW con-
trols were selected. The LBW rate
among women with private dental in-
surance was 3.8%, or 0.7% lower than
the LBW rate (4.5%) for Washington
State during the same period
(1993-2000). When compared with all
women who had live births in Wash-
ington State, women who had private
dental insurance were on average 1.5
years older (28.8 vs 27.3 years), more
educated (14.3 years vs 12.9 years),
smoked less (7.5% vs 14.6%), and were
more likely to be white (81% vs 73%).
The use of dental diagnostic radiog-
raphy was independent of several risk
factors for LBW. Dental diagnostic ra-
diation dose was not related to mater-
nal age (P = 0.00, P = .90), diabetes
(P = 0.00, P = .88), self-reported alcohol
consumption (P = 0.00, P = .79), num-
ber of prenatal visits (P = 0.02, P = .90),
chronic hypertension (P = 0.01, P = .52),
or preeclampsia (P = −0.01, P = .72).
Women reporting cigarette smoking had
on average a 0.01 mGy higher radiation
dose than women reporting not smok-
ing (P = .14). Women with inadequate
pregnatal care had on average 0.05 mGy
more radiation exposure than women
with adequate prenatal care (P = .13).
Ethnicity was related to dental radiation
doses (P = .01), with women of Asian eth-
iceity having a mean radiation dose of
0.05 mGy, black women having a radia-
tion dose of 0.04 mGy, and white women
having a radiation dose of 0.03 mGy.
Dental radiation exposures were more
common among women with LBW in-
fants than among women with NBW in-
fants. Among the women who deliv-
ered a LBW infant, 1.9% (n = 21) had
higher than 0.4 mGy radiation, as op-
posed to 1.0% of the women with NBW
infants (P = .02) (TABLE 2). Among the
women who delivered a TLBW infant,
the prevalence of the higher than 0.4
mGy radiation dose was 3.0% (n = 10),
which was also significantly higher than
among controls (P = .002). The prev-
ance of the higher than 0.4 mGy radia-
tion dose among women with a PLBW
infant and a VLBW infant was 1.6% and
1.0%, respectively, which was not sig-
nificantly different from the prev-
ance in women with NBW infants
(P = .24 and P > .99, respectively). Estab-
lished risk factors for LBW such as ma-
terial age, diabetes, smoking, ethnic-
ity, preeclampsia, chronic hypertension,
prepregnancy weight, maternal weight
gain, and parity were significantly asso-
ciated with LBW in the studied popu-
lation (Table 1).
When compared with women with no
known dental diagnostic radiography,
a thyroid radiation dose of more than 0.4
mGy increased the adjusted odds for
LBW by 2.27 (95% confidence interval
[CI], 1.11-4.66) (TABLE 3). A thyroid ra-
diation dose of 0.1 to 0.4 mGy was as-
sociated with an adjusted OR of 1.20
When radiation dose was modeled as a continuous variable, a 1-mGy increase was associated with a 1.83 increased odds for a LBW infant (95% CI, 1.10-3.04). Further adjustment of the OR for the different types of dental procedures performed during pregnancy did not affect the radiation-LBW association (Table 3).

Table 1. Characteristics of Women Giving Birth to Low-Birth-Weight (LBW) Infants, Term Low-Birth-Weight (TLBW) Infants, and Normal-Birth-Weight (NBW) Infants*

<table>
<thead>
<tr>
<th>Maternal Characteristics</th>
<th>LBW Infants (n = 1117)</th>
<th>TLBW Infants (n = 336)</th>
<th>NBW Infants (n = 4468)</th>
<th>( P ) Value, LBW vs NBW†</th>
<th>( P ) Value, TLBW vs NBW</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
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<td></td>
<td></td>
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<tr>
<td>&lt;20</td>
<td>190 (17.0)</td>
<td>51 (15.2)</td>
<td>483 (10.8)</td>
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<td>.01</td>
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<td>20-24</td>
<td>200 (17.9)</td>
<td>64 (19.0)</td>
<td>750 (16.8)</td>
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<td>.31</td>
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<tr>
<td>25-29</td>
<td>192 (17.2)</td>
<td>65 (19.3)</td>
<td>1025 (22.9)</td>
<td>&lt;.001</td>
<td>.13</td>
</tr>
<tr>
<td>30-34</td>
<td>282 (25.2)</td>
<td>82 (24.4)</td>
<td>1287 (28.8)</td>
<td>.04</td>
<td>.10</td>
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<tr>
<td>35-39</td>
<td>193 (17.3)</td>
<td>53 (15.8)</td>
<td>752 (16.8)</td>
<td>.98</td>
<td>.55</td>
</tr>
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<td>≥40</td>
<td>60 (5.4)</td>
<td>21 (6.3)</td>
<td>171 (3.8)</td>
<td>.02</td>
<td>.03</td>
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<td><strong>Ethnicity</strong></td>
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<td>White</td>
<td>813 (72.8)</td>
<td>255 (75.9)</td>
<td>3644 (81.6)</td>
<td>&lt;.001</td>
<td>.02</td>
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<td>Black</td>
<td>83 (7.4)</td>
<td>17 (5.1)</td>
<td>142 (3.2)</td>
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<td>.05</td>
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<tr>
<td>Asian</td>
<td>96 (8.6)</td>
<td>26 (7.7)</td>
<td>298 (6.7)</td>
<td>.16</td>
<td>.08</td>
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<tr>
<td>Other</td>
<td>125 (11.2)</td>
<td>38 (11.3)</td>
<td>384 (8.6)</td>
<td>.01</td>
<td>.10</td>
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<td><strong>Education</strong></td>
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<tr>
<td>&gt;12 y</td>
<td>620 (55.5)</td>
<td>195 (57.5)</td>
<td>2902 (65.0)</td>
<td>&lt;.001</td>
<td>.008</td>
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<tr>
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<td>156 (14.0)</td>
<td>33 (9.8)</td>
<td>373 (8.4)</td>
<td>&lt;.001</td>
<td>.35</td>
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<td><strong>Kessner Adequacy of Prenatal Care Index</strong></td>
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<tr>
<td>Adequate</td>
<td>677 (60.6)</td>
<td>237 (70.5)</td>
<td>3261 (73.0)</td>
<td>&lt;.001</td>
<td>.31</td>
</tr>
<tr>
<td>Intermediate</td>
<td>299 (26.8)</td>
<td>70 (20.8)</td>
<td>876 (19.6)</td>
<td>&lt;.001</td>
<td>.60</td>
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<tr>
<td>Inadequate</td>
<td>27 (2.4)</td>
<td>3 (0.9)</td>
<td>34 (0.8)</td>
<td>&lt;.001</td>
<td>.79</td>
</tr>
<tr>
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<td>114 (10.2)</td>
<td>26 (7.7)</td>
<td>297 (6.6)</td>
<td>&lt;.001</td>
<td>.39</td>
</tr>
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<td><strong>Marital status</strong></td>
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<tr>
<td>Not married</td>
<td>295 (26.4)</td>
<td>85 (25.3)</td>
<td>843 (18.9)</td>
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<td>.004</td>
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<tr>
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<td>1 (0.3)</td>
<td>6 (0.1)</td>
<td>.72</td>
<td>.46</td>
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<td><strong>Dental insurance eligibility during pregnancy, mean (SE), No. of wk</strong></td>
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<td>Yes</td>
<td>12.1 (0.2)</td>
<td>12.7 (0.3)</td>
<td>14.8 (0.1)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>394 (35.3)</td>
<td>83 (24.7)</td>
<td>1147 (25.7)</td>
<td>&lt;.001</td>
<td>.79</td>
</tr>
<tr>
<td><strong>Prepregnancy weight, mean (SE), kg</strong></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>64.0 (0.6)</td>
<td>62.0 (0.9)</td>
<td>66.3 (0.3)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>421 (37.7)</td>
<td>95 (28.3)</td>
<td>1199 (26.8)</td>
<td>&lt;.001</td>
<td>.57</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Established or gestational</td>
<td>46 (4.1)</td>
<td>10 (3.0)</td>
<td>114 (2.6)</td>
<td>.005</td>
<td>.51</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>105 (9.4)</td>
<td>20 (6.0)</td>
<td>371 (8.3)</td>
<td>.24</td>
<td>.13</td>
</tr>
<tr>
<td><strong>Parity</strong></td>
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</tr>
<tr>
<td>0</td>
<td>742 (66.4)</td>
<td>236 (70.2)</td>
<td>2393 (53.6)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1-2</td>
<td>280 (25.1)</td>
<td>76 (22.6)</td>
<td>1699 (38.0)</td>
<td>.08</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>≥3</td>
<td>45 (4.0)</td>
<td>10 (3.0)</td>
<td>210 (4.7)</td>
<td>.37</td>
<td>.14</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>50 (4.5)</td>
<td>14 (4.2)</td>
<td>166 (3.7)</td>
<td>.28</td>
<td>.65</td>
</tr>
<tr>
<td><strong>Self-reported No. of alcoholic drinks per wk ≥1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19 (1.7)</td>
<td>5 (1.5)</td>
<td>63 (1.4)</td>
<td>.44</td>
<td>.76</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>156 (14.0)</td>
<td>35 (10.4)</td>
<td>421 (9.4)</td>
<td>&lt;.001</td>
<td>.51</td>
</tr>
<tr>
<td><strong>Self-report of smoking during pregnancy</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>140 (12.5)</td>
<td>52 (15.5)</td>
<td>325 (7.3)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>62 (5.6)</td>
<td>13 (3.9)</td>
<td>140 (3.1)</td>
<td>&lt;.001</td>
<td>.46</td>
</tr>
<tr>
<td><strong>Preeclampsia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>149 (13.3)</td>
<td>49 (14.6)</td>
<td>222 (5.0)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
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<td>105 (9.4)</td>
<td>20 (6.0)</td>
<td>371 (8.3)</td>
<td>.24</td>
<td>.13</td>
</tr>
<tr>
<td><strong>Chronic hypertension</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39 (3.5)</td>
<td>11 (3.3)</td>
<td>28 (0.6)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Information unavailable</td>
<td>105 (9.4)</td>
<td>20 (6.0)</td>
<td>371 (8.3)</td>
<td>.24</td>
<td>.13</td>
</tr>
</tbody>
</table>

*Data are expressed as number (percentage) unless otherwise indicated. Weight categories: LBW, less than 2500 g; TLBW, 1501 to 2499 g and 37 or more menstrual weeks of gestation; NBW, at least 2500 g.

†All \( P \) values estimated using an exchangeable correlation matrix, except for prepregnancy weight where an independence correlation structure was used.
Table 2. Dental Procedure Characteristics of Women Giving Birth to Low-Birth-Weight (LBW) Infants, Term Low-Birth-Weight (TLBW) Infants, and Normal-Birth-Weight (NBW) Infants*

<table>
<thead>
<tr>
<th>Dental Procedure Characteristics</th>
<th>LBW Infants (n = 1117)</th>
<th>TLBW Infants (n = 336)</th>
<th>NBW Infants (n = 4468)</th>
<th>P Value, LBW vs NBW</th>
<th>P Value, TLBW vs NBW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated dental-related thyroid exposure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.4 mGy (mean, 1.2 mGy)</td>
<td>21 (1.9)</td>
<td>10 (3.0)</td>
<td>46 (1.0)</td>
<td>.02</td>
<td>.002</td>
</tr>
<tr>
<td>0.1-0.4 mGy (mean, 0.2 mGy)</td>
<td>112 (10.0)</td>
<td>39 (11.6)</td>
<td>419 (9.4)</td>
<td>.52</td>
<td>.17</td>
</tr>
<tr>
<td>0 mGy (no known dental radiography)</td>
<td>984 (88.1)</td>
<td>287 (85.4)</td>
<td>4003 (89.6)</td>
<td>.16</td>
<td>.02</td>
</tr>
<tr>
<td>Full-mouth dental radiography</td>
<td>11 (1.0)</td>
<td>4 (1.2)</td>
<td>28 (0.6)</td>
<td>.20</td>
<td>.23</td>
</tr>
<tr>
<td>≥1 Panoramic radiograph†</td>
<td>21 (1.9)</td>
<td>7 (2.1)</td>
<td>42 (0.9)</td>
<td>.009</td>
<td>.05</td>
</tr>
<tr>
<td>Bitewings, mean (SE), No.</td>
<td>0.30 (0.03)</td>
<td>0.37 (0.06)</td>
<td>0.25 (0.01)</td>
<td>.12</td>
<td>.05</td>
</tr>
<tr>
<td>Periapical radiographs, mean (SE), No.</td>
<td>0.07 (0.01)</td>
<td>0.11 (0.02)</td>
<td>0.06 (0.01)</td>
<td>.27</td>
<td>.02</td>
</tr>
<tr>
<td>Total No. of dental procedures per 100 women per year</td>
<td>259.4</td>
<td>328.7</td>
<td>287.4</td>
<td>.02</td>
<td>.08</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>108.0</td>
<td>130.6</td>
<td>116.9</td>
<td>.07</td>
<td>.10</td>
</tr>
<tr>
<td>Preventive</td>
<td>87.1</td>
<td>103.9</td>
<td>102.5</td>
<td>&lt;.001</td>
<td>.83</td>
</tr>
<tr>
<td>Restorative</td>
<td>35.4</td>
<td>50.1</td>
<td>43.1</td>
<td>.13</td>
<td>.49</td>
</tr>
<tr>
<td>Endodontic</td>
<td>3.3</td>
<td>5.5</td>
<td>3.0</td>
<td>.68</td>
<td>.04</td>
</tr>
<tr>
<td>Periodontal</td>
<td>10.0</td>
<td>12.3</td>
<td>11.8</td>
<td>.41</td>
<td>.89</td>
</tr>
<tr>
<td>Removable prosthodontic</td>
<td>0.3</td>
<td>0.8</td>
<td>0.3</td>
<td>.88</td>
<td>.19</td>
</tr>
<tr>
<td>Implants and fixed prosthodontic</td>
<td>0.8</td>
<td>1.3</td>
<td>0.7</td>
<td>.91</td>
<td>.56</td>
</tr>
<tr>
<td>Oral surgery</td>
<td>6.7</td>
<td>12.7</td>
<td>5.6</td>
<td>.66</td>
<td>.17</td>
</tr>
<tr>
<td>Orthodontic</td>
<td>7.8</td>
<td>11.5</td>
<td>3.5</td>
<td>.05</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviation: mGy, milligray.
*Data are expressed as number (percentage) unless otherwise indicated. Weight categories: LBW, less than 2500 g; TLBW, 1501 to 2499 g and 37 or more menstrual weeks of gestation; NBW, at least 2500 g.
†One woman had 2 panoramic radiographs during gestation.

Subsequently, the association between diagnostic radiation and different types of LBW outcomes was evaluated. There was no significant association between a radiation dose higher than 0.4 mGy and the OR for VLBW infants (OR, 2.19; 95% CI, 0.21-22.49) or the OR for PLBW infant (OR, 1.77; 95% CI, 0.65-4.78).

There was a strong association between diagnostic radiation and TLBW infants (Table 3). When the thyroid radiation dose was higher than 0.4 mGy, the adjusted OR for a TLBW infant was 3.61 (95% CI, 1.46-8.92) when compared with women with no known dental radiography. When the radiation dose to the thyroid was 0.1 to 0.4 mGy, the adjusted OR for a TLBW infant was 1.66 (95% CI, 1.09-2.53). Further adjustment of the OR for the different types of dental procedures performed during pregnancy did not affect the OR (Table 3). When the cumulative radiation dose was modeled as a continuous variable, a 1-mGy increase was associated with a 2.59 increased odds for a TLBW infant (95% CI, 1.37-4.90) after adjustment for confounding variables. When values were imputed for missing confounders, the OR for a TLBW infant associated with a radiation dose to the thyroid higher than 0.4 mGy was 2.89 (95% CI, 1.32-6.33) when compared with women with no known dental radiography.

Subgroup analyses showed strong associations among women with adequate prenatal care or women reporting not smoking. Thyroid radiation higher than 0.4 mGy in nonsmokers was strongly associated with TLBW infants (naive OR, 4.81; 95% CI, 1.81-12.79). The naive OR estimate among women reporting smoking during pregnancy was 1.61 (95% CI, 0.15-17.34). Among women with adequate prenatal care, thyroid radiation higher than 0.4 mGy was associated with an OR for a TLBW infant of 4.38 (95% CI, 1.79-10.74) when compared with women with no known dental radiography.

Over two thirds of the total radiation doses (70.5%) were received in the first trimester. During the first trimester, a radiation dose higher than 0.4...
mGy was associated with an OR for a LBW infant of 3.11 (95% CI, 1.44-6.73) and the OR for a TLBW infant was 5.49 (95% CI, 2.12-14.17). During the second and third trimester, the confidence limits around the OR were too wide to make meaningful inferences.

COMMENT

In this study, antepartum dental radiography in pregnant women was associated with an increased risk for a LBW infant, especially a TLBW infant. The prevalence of dental radiography during pregnancy in this dentally insured population was approximately 10%. Since women may not always be aware of their pregnancy status, it may not be possible to eliminate all dental radiography during pregnancy, but if this goal could be achieved and if the identified association is causal, the prevalence of TLBW infants could be reduced by up to 5%. Current guidelines for diagnostic radiography, which are based on the notion that only direct radiation to the reproductive organs is of concern during pregnancy, may need to be evaluated further.

While the findings of this study cannot determine which organ in the head-and-neck region may be responsible for the observed radiation-LBW association, epidemiological and experimental evidence point to the thyroid. Very low-dose radiation has been associated with thyroid dysfunction such as thyroid autonomy in young females, thyroid cysts in females of all ages, and papillary thyroid cancer among multiparous women. The thyroid's susceptibility to radiation has been hypothesized to be high during pregnancy. In addition to the evidence on radiation-induced thyroid dysfunction, there is evidence that subtle, subclinical thyroid dysfunction decreases birth weight and delays neurointellectual development of the offspring. This raises the possibility that radiation-induced thyroid dysfunction may also affect the neurointellectual development of the offspring. Low-dose radiation in utero leads to poor performance on intelligence tests. While those associations have typically been attributed to the direct effects of radiation on the development of the brain, the potential role of radiation-induced thyroid dysfunction on brain development may need to be further explored.

Strengths of this study include the unbiased selection of cases and controls from registries, the individual radiation dosimetry data, the absence of recall bias with respect to radiation between cases and controls, the control for well-established risk factors of LBW, and the validation of the insurance records with respect to dental radiography information. Such rigor in design has often been difficult to achieve when studying the effects of radiation on pregnancy outcomes. In prior studies, birth weight was often assessed by maternal recall, selection bias was difficult to control due to nonresponse or survival bias, and bias due to confounding from the lack of information on other risk factors for LBW, such as diabetes, chronic hypertension, or smoking, could not always be adjusted for.

Several factors reduced the potential for residual confounding. First, because all women had private dental insurance, the selected sample was of a higher and more homogeneous socioeconomic class (eg, higher education) and had better health awareness (eg, lower smoking prevalence) than the population of Washington State. Such restriction in subject selection is a useful tool to control confounding. However, such restriction had the disadvantage that it limited the ability to assess effect modification—the number of women in certain subgroups, such as women reporting smoking or women with inadequate prenatal care, was too sparse to provide meaningful inference. Second, dental radiography doses were not related to important risk factors of LBW such as maternal age, diabetes, preeclampsia, and chronic hypertension. Third, among women exposed during the first trimester, when radiation has been reported to have the greatest effect on infant growth, the OR for TLBW was 5 and the lower limit of the 95% CI excluded 2. Odds ratios of such size are less likely to be the result of residual confounding.

Weaknesses of the study include potential measurement errors of confounders such as smoking, the lack of thyroid function measures, the lack of information on nondental radiation exposures, bias in the linking process, the possibility of a chance finding, and missing data. It is possible that underreporting of the socially undesirable behavior of smoking during pregnancy biased the association between dental radiography and LBW. It is unclear to what extent restricting the analyses to women reporting not smoking minimized bias since attendants may be more likely to note smoking on a birth certificate for a LBW infant than for a NBW infant. Some control for smoking was obtained by restricting the study population to those women of higher socioeconomic class in whom smoking prevalence is lower. The lack of thyroid function measures in the current study eliminated our ability to determine if indeed the thyroid is involved in explaining the observed association.

The likelihood of matching mothers' names may have depended on ethnicity, which may have induced selection biases because ethnicity was related to both radiation dose and birth weight. This bias may have been minimized, but not eliminated, by controlling for ethnicity and ethnicity-related risk factors for LBW, such as diabetes. The reported results may be a chance finding, but this is less likely given that prior studies also identified associations between diagnostic radiation and LBW. The prevalence of missing data for certain confounders was moderately high. Even though imputation for missing values did not substantially influence the results, it is possible that the missing data biased the results.

The impact of nondental radiation or factors associated with dental radiography on the reported study findings is unknown. Additional analyses of data from a population-based case-control study on dental radiation suggested that nondental therapeutic or diagnostic radia-
tion during pregnancy is of low prevalence. It is possible that extensive dental radiography is associated with certain conditions such as facial trauma, tumors, or dental diseases, which in this study may have increased the risk for adverse pregnancy outcomes and caused a spurious association between radiation and LBW. Since adjustment for treatments of dental diseases did not affect the ORs, the possibility for dental diseases or treatments to confound the association is diminished but not eliminated. Furthermore, the observation that both orthodontic and endodontic therapies, 2 procedures where diagnostic radiation is common, were associated with TBLBW is more suggestive of dental radiography being associated with TBLBW than dental diseases or procedures.

In summary, this study provides evidence that very low-dose radiation to the maternal head-and-neck region during pregnancy is associated with LBW offspring. If indeed the hypothalamic-pituitary-thyroid axis is somehow involved in the causal pathway, it is possible that a further understanding of disease mechanisms may lead to new intervention strategies for those circumstances where avoidance of very low-dose radiation is difficult. The notion that very low-dose radiation exposures to nonreproductive organs in expectant mothers are safe needs to be investigated further.

Author Contributions: As principal investigator, Dr Hujoel had full access to all of the data in the study and takes full responsibility for the integrity of the data and the accuracy of the analyses.

Study concept and design: Hujoel, Bollen, del Agua. Acquisition of data: Hujoel, del Agua. Analysis and interpretation of data: Hujoel, Bollen, Noonan, del Agua.

Drafting of the manuscript: Hujoel, Bollen. Critical revision of the manuscript for important intellectual content: Hujoel, Bollen, Noonan, del Agua. Statistical expertise: Hujoel, Noonan, del Agua. Obtained funding: Hujoel. Administrative, technical, or material support: Hujoel, Bollen, del Agua.

Supervision: Hujoel, Bollen.

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Role of the Sponsor: The major funding organization, the Washington Dental Service Foundation, reviewed and approved the research proposal entitled “Mother-Child Dental Utilization and Low Birth Weight.” This funding organization had no influence on the design or conduct of the study, or the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

The manuscript that was sent to JAMA for consideration was also sent to the Washington Dental Service for their records. Human subject approval was obtained on the condition that no members of Washington Dental Service could analyze those data where dental service utilization was linked to birth certificate data.

Acknowledgment: We thank the Washington State Department of Health for access to vital records data for this project, and Bill O’Brien from the Department of Epidemiology at the University of Washing- ton and James Foster from Washington Dental Service for assistance with programming and data linkage. We also thank Mark Drangsholt, DDS, MPH, for his comments and suggestions.

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5. Hamilton PM, Roney PL, Keppel KG, Placek PJ. Radiation exposures to nonreproductive organs in dental patients during pregnancy is of low prevalence. Antepartum dental radiography and infant low birth weight. This funding organization had no influence on the design or conduct of the study, or the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

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