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Maternal Exposure to Radiographic Exams and Major Structural Birth Defects

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Abstract

Background—An increasing number of radiologic exams are performed in the United States, but very few studies have examined the effects of maternal exposure to radiologic exams during the periconceptional period and birth defects.

Objectives—To assess the association between maternal exposure to radiologic exams during the periconceptional period and 19 categories of birth defects using a large population-based study of birth defects. Methods: We studied 27,809 case mothers and 10,200 control mothers who participated in the National Birth Defects Prevention Study and delivered between 1997 and 2009. Maternal exposure to radiologic exams that delivered ionizing radiation to the urinary tract, lumbar spine, abdomen, or pelvis were identified based on the mother's report of type of radiologic exams, organ or body part scanned and the month during which the exam occurred

Results—Overall, 0.9% of mothers reported exposure to one of these types of radiographic exams during the periconceptional period. We observed significant associations between maternal exposure during the first trimester and isolated Dandy-Walker malformation (odds ratio = 7.7; 95% confidence interval, 1.8–33) and isolated d-transposition of the great arteries (odds ratio = 3.8; 95% confidence interval, 1.4–10.3). However, the result for isolated Dandy-Walker malformation was based on only two exposed cases.

Conclusion—These results should be interpreted cautiously because multiple statistical tests were conducted and measurements of exposure were based on maternal report. However, our results may be useful for generating hypotheses for future studies.

Keywords

birth defects; isolated d-transposition of the great arteries; radiography

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Introduction

Radiologic exams are used to diagnose and treat diseases. However, at sufficient levels, ionizing radiation (IR) exposure has been associated with cancer and gene mutations (De Santis et al., 2005; Herdt-Losavio et al., 2010). In addition, a report by the National Academy of Science concluded that the condition that is most likely to be caused by exposure to IR is multiple anomalies of the newborn (Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII, 2006).

In recent decades, the dosage of IR used in radiologic exams has decreased substantially, however, the frequency of radiologic exams has been increasing in the United States (National Council on Radiation and Measurements, 2009, 2012; National Institute for Occupational Safety and Health). Fazel et al. observed that 53.4% of U.S. women and 45.2% of U.S. men aged 18 to 34 reported having at least one radiologic exam during a 3-year period (Fazel et al., 2009).

One population-based study assessed maternal reports of exposure to radiologic exams during the periconceptional period and congenital heart defects in aggregate including 4390 cases of heart defects and 3572 controls (Ferencz et al., 1993). They observed no significant associations between maternal reports of abdominal x-rays and all congenital heart defects in aggregate (odds ratio [OR] = 0.77; 95% confidence interval [CI], 0.47–1.27).

Our objective in this study was to evaluate the assumption that levels of IR present in radiologic exams in the United States are sufficiently low that they do not cause birth defects. Using data from the National Birth Defects Prevention Study (NBDPS), we examined the effects of maternal exposure to radiographic exams during the periconceptional period and specific birth defects.

Materials and Methods

Study Population

The NBDPS is a case–control study with 10 participating sites: Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah. Infants or fetuses who were delivered between October 1, 1997, and December 31, 2009, were eligible for the current analysis. For the majority of participating sites, cases were live-born infants, fetal deaths of at least 20 weeks' gestation and elective pregnancy terminations of any gestational age. Controls were live-born infants without major birth defects, randomly selected from birth certificates or birth hospitals to represent the birth population from which the cases were drawn. This study was approved by the institutional review boards of each of the participating study sites and the Centers for Disease Control and Prevention. Detailed study methods have been published previously (Yoon et al., 2001; Rasmussen et al., 2003).

All cases were reviewed by clinicians affiliated with the NBDPS according to established guidelines and were classified as having isolated, multiple, or complex birth defects (Rasmussen et al., 2003). Cases with isolated birth defects were defined as having either one major birth defect, two or more major birth defects affecting only one organ system, or one

major birth defect with a sequence of related defects. Cases with multiple birth defects had two or more major unrelated defects in different organ systems. Birth defects that were known or strongly suspected to have been caused by single-gene disorders or chromosomal abnormalities were excluded from the NBDPS. Utah was unable to contribute cases of orofacial clefts in 2003; California only began to contribute cases of pulmonary valve stenosis beginning on January 1, 2002; and cases of congenital cataracts were only contributed study-wide beginning January 1, 2000. For calculations involving these birth defects, we excluded information from control mothers for those locations and study periods during which cases were not available. As all cases of hypospadias were male, for analyses of hypospadias, we restricted controls to the mothers of male infants.

Exposure Assessment

Maternal interviews were conducted using a standardized, computer-assisted telephone interview in English or Spanish within 24 months of delivery. Interviews were completed within an average of 11 months from the estimated date of delivery for cases, and 9 months for controls, which allowed for sufficient time for identification of cases and abstraction and review of medical records.

As radiographic exams deliver exposures that are narrowly focused on the organ of interest, with extremely low levels of exposure to tissues surrounding the organ of interest, we chose to focus our study on radiographic exams of the urinary tract, lumbar spine, abdomen, or pelvis, which deliver the highest levels of exposure to the fetus or pelvis. We also coded mothers as exposed if they had hysterosalpingograms or radiographic exams in which the entire body was exposed to IR (nuclear medicine exam and whole-body positron emission tomography scans).

Estimates of the average level of pelvic or fetal exposure delivered by these types of radiographic exams ranged from a low of 1 mGy for a conventional x-ray of the abdomen (Damilakis et al., 2002; Lazarus et al., 2009; Health Physics Society Specialists in Radiation Safety, 2010; Wallace, 2011; Osei and Darko, 2012) to a high of 25 mGy for a pelvic computed tomography (CT) scan (Angel et al., 2008; Chen et al., 2008). It is important to note that the exam with the highest level of exposure, that is, a pelvic CT scan, is associated with levels of IR below the threshold of safety for fetal exposures to IR from radiographic exams, which is 50 mGy (Centers for Disease and Prevention). However, pelvic CT scans are sometimes performed once with contrast and then again without contrast. In such cases, the fetal dose will be approximately double or 50 mGy. In comparison, the average fetal dosages of IR for examples of those radiographic exams that we chose not to classify as exposed are < 0.06 mGy for a chest CT, < 0.05 mGy for mammography, < 0.01 mGy for an x-ray of the extremities, < 0.005 mGy for a CT of the head and neck, and < 0.001 mGy for dental x-rays (Yang et al., 1992; Russell et al., 1997; International Commission on Radiological Protection (ICRP), 2000; Lowe, 2004; McCollough et al., 2007; Sulieman et al., 2008; The Agency for Clinical Innovation, 2015). These radiographic exams, which are focused on areas of the body other than the urinary tract, lumbar spine, abdomen, or pelvis were excluded from analysis.

The section of the interview on radiographic exams asked mothers to report any “x-rays or scans not related to their pregnancy.” If they answered yes, for each scan they were asked to indicate whether it was an x-ray, a CT scan, an MRI scan, a nuclear medicine study, or “other x-ray or scan.” Although, the question was not intended to capture ultrasound exams related to the pregnancy, some were reported under other x-ray or scan. Mothers were also asked to report the organ or body part that was scanned and the month in which each type of exam occurred. This information was collected on up to five exams for each woman. There were 686 mothers who reported that they had “other x-rays or scans.” These mothers were asked to give additional details on the type of scan in an open ended text file.

The lead author (H.L.) reviewed the answers from the open text questions and coded them as exposed or not. The coding of the open text questions was reviewed by one of the authors who has 20 years of experience as an epidemiologist with an additional 7 years of experience working in a hospital as a registered nurse (D.K.W.) and a few answers that these two reviewers did not agree on were reviewed by a hospital based health physicist with 20 years of experience (C.W.B.). Of 686 mothers, 116 mothers reported a specific type of radiologic exam, time in gestation and the organ or body part that it occurred. Thus, their answers were coded as exposed or not. The remaining 570 mothers’ answers were coded as missing in the analysis because they gave a poor or incomplete description of a radiologic exam or they did not include the organ or body part that was scanned or the timing of the exam.

The biologic mechanism by which exposure to IR may cause birth defects is likely to vary depending on whether the exposure occurs in the period after conception or in the period immediately before conception. After conception, the embryo is present and IR may cause birth defects by means of cell damage in the embryo or mutations in the embryonic DNA. Before conception, IR may induce birth defects by means of DNA damage in the ovum (Kirk and Lyon, 1984; Marchetti et al., 2001; De Santis et al., 2005; Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII, 2006; Xu et al., 2008). Because of these differences, we categorized exposed mothers for two separate time periods: (1) exposed to IR between the 3 months immediately before and conception, and (2) exposed to IR between conception and the 3 months immediately after conception.

Statistical Analysis

When we assessed the association between maternal exposure to IR during the 3 months before conception and birth defects, mothers who were exposed for only this time period and mothers who were unexposed for any time periods were included in analysis. Likewise, for the assessment of the association between maternal exposure during the first trimester and birth defects, any mothers who were exposed only in the first trimester and mothers who were unexposed for any other times were included in analysis. These exclusions were made to prevent errors in the timing of these exposures from affecting the results.

We initially assessed the association between these two exposure categories and all birth defects in aggregate and 10 broad categories of birth defects. For noncardiac defects, these groups were based primarily on organ systems. For cardiac defects, we used categories

defined by clinicians affiliated with the NBDPS (Botto et al., 2007). This was done so that we could compare our results with studies that used similarly broad categories.

For the analyses of individual categories of birth defects, we restricted the sample to isolated cases. This was done to create mutually exclusive groups for interpretation of multiple statistical tests.

Among the birth defect phenotypes included in the NBDPS, we assessed 19 categories of isolated birth defects that had ≥ 2 or more exposed cases before multivariable adjustments for either of the two time periods that we studied. This was done because those phenotypes with fewer cases would not have allowed estimation of sufficiently precise ORs.

As a report by the National Academy of Science suggested that IR might be associated with infants with multiple birth defects (De Santis et al., 2005; Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII, 2006), we also assessed the relationship between exposure to IR and nonisolated or multiple birth defects. For that purpose, we collapsed all nonisolated birth defects into one category.

Among women who were exposed to radiographic exams of interest, there remained a wide range in the levels of exposure. In Table 3, we addressed this by stratifying mothers in this group by the type of radiologic exams that they were exposed to: (1) nuclear medicine; (2) CT of the pelvis; (3) CT of the lumbar spine; (4) CT of the abdomen; (5) hysterosalpingogram; (6) intravenous pyelogram or x-ray of the kidneys, ureters, and bladder; (7) conventional x-ray of pelvis, lumbar spine, or abdomen; (8) total-body positron emission tomography scan; and (9) more than one of radiologic exam. To achieve sufficient statistical power to assess the effect of different types of radiologic exams, we collapsed all birth defects in the NBDPS study into one group for the analyses in Table 3.

Logistic regression was used to examine ORs for all associations in this study (Tables 2 and 3). When the number of exposed cases remaining after adjustments was >1 and <5, we reported crude odds ratio (COR), because when a cell has four observations or less, adjustment by multiple factors is likely to be less accurate than the COR (Greenland, 2000). When fewer than two exposed cases remained after adjusting, we did not report the odds ratios. Our criteria for borderline significance were a lower confidence interval of 0.95 to 1.0, and our criteria for statistical significance was a lower confidence interval of > 1.0.

We assessed the possibility of confounding from the following characteristics gathered from the maternal interview: maternal age at delivery, race, level of education, prepregnancy body mass index (BMI), pre-existing diabetes, smoking, use of supplements containing folic acid, any consumption of alcohol, use of illicit drugs, household income, first live birth, injury not related with pregnancy, and study location. We ran backward logistic regression models separately for each of the birth defects in Table 2. Variables that resulted in a change in the OR of 10% or more for any category were considered to be confounders and were retained in all of our final models. Based on this criterion, all of our final models were adjusted for study site, household income, preexisting diabetes, injury, any smoking, and maternal BMI. The format for the variables that were entered into the final models is shown in Table 1. All

analyses were performed using the statistical software package SAS (release 9.3, SAS Institute, Cary, NC).

Results

After excluding 17 mothers with any lifetime history of radiotherapy or cancer, and 349 mothers who did not indicate whether they had radiologic exams or not, our study included 37,643 mothers who ever had personal radiographic exams between 3 months before conception and the end of the first trimester of pregnancy and who participated in the NBDPS between 1997 and 2009 (27,535 mothers of infants with birth defects and 10,108 mothers of infants without birth defects). Participation among NBDPS cases and controls for the years 1997 to 2009 was 70% and 66%, respectively.

Table 1 shows the frequency of selected characteristics of cases and controls. Compared with control mothers, case mothers were more likely to be 35 years of age or older, smokers, overweight or obese, diabetic, or giving birth to their first child. Cases were less likely to have a household income of $50,000 or more and less likely to be college graduates.

Overall, 0.92% and 0.83% of study participants were exposed to radiographic exams during the periconceptional period that were directed at the urinary tract, lumbar spine, abdomen, or pelvis (Table 1). There were no significant or borderline significant associations between mothers who had these types of exams during 3 months before conception and all birth defects in aggregate, any of the 10 broad categories of birth defects, nor any of the 19 isolated birth defects (Table 2).

For exposures occurring during the first trimester, the OR for all birth defects in aggregate was not elevated; however, the odds ratios for 2 of the 10 broad groups of birth defects were elevated and borderline significant; central nervous system defects, and conotruncal defects (adjusted odds ratio [AOR] = 2.74; 95% CI, 0.96 – 7.84), and (AOR = 2.12; 95% CI, 0.98–4.60), respectively (Table 2). For the other broad groups of birth defects, we observed no odds ratios that were elevated and significant or borderline significant.

Also, mothers who were exposed to these radiologic exams during the first trimester had significantly elevated ORs for 2 of the 19 isolated birth defects assessed in Table 2: isolated Dandy-Walker malformation (COR = 7.73; 95% CI, 1.81–33.0) and isolated d-transposition of the great arteries (AOR = 3.85; 95% CI, 1.45–10.3). There was no association between mothers who were exposed to these type of radiographic exams and all nonisolated birth defects in aggregate during either of the two periconceptional periods that we assessed (AOR = 1.20; 95% CI, 0.72–2.03) and (AOR = 1.07; 95% CI, 0.51–2.23).

There were no significant or borderline significant associations between any of nine subtypes of radiologic exams and all birth defects in aggregate (Table 3). For exposure to intravenous pyelogram or x-rays of the kidneys, ureters, and bladder occurring between 3 months before conception and conception, there was an elevated OR that was not significant and lacked precision (AOR = 2.21; 95% CI, 0.49–9.86). In addition, for exposure to a CT scan of the abdomen during the first trimester, there was an elevated OR that was also not significant and lacked precision (AOR = 3.46; 95% CI, 0.44–27.1).

Discussion

This study examined the relationship between maternal reports of exposure to radiologic exams of the urinary tract, lumbar spine, abdomen, or pelvis, all of which deliver an average pelvis or fetal exposure to IR of 1.0 mGy or more, and 19 specific categories of birth defects. For exposure during the first trimester, we observed significantly elevated ORs for two birth defects: isolated Dandy-Walker malformation and isolated d-transposition of the great arteries with *p*-value of 0.005, and 0.007, respectively. However, these ORs did not remain significant when we used a Bonferroni adjustment to determine the cut-point for a significant *p*-value (0.05/19 = 0.002). We also found no association for exposure to radiologic exams in either of the exposure windows and all nonisolated birth defects in aggregate, based on 22 cases exposed before conception and 11 cases exposed after conception.

The Baltimore–Washington infant study, conducted between 1981 and 1989 (Ferencz et al., 1993) was a U.S. population-based case control study that assessed the association between maternal exposure to radiologic exams between 3 months before conception and end of the first trimester based on maternal interview and all heart defects in aggregate. This study included 4390 cases of heart defects and observed no significant associations between maternal reports of abdominal x-rays during the periconceptional period and all congenital heart defects in aggregate (OR = 0.77; 95% CI, 0.47–1.27). Our finding of no association between mothers with exposure to conventional x-rays of pelvis, lumbar spine, or abdomen and all birth defects in aggregate is consistent with the results of this study, although our estimate is based on all cardiac and noncardiac birth defects. The Baltimore–Washington study did not describe any exposures to CT scans, which generally deliver much higher levels of exposures, but would have been less common during the time period of that study.

Korean investigators followed 115 pregnant women who were exposed to abdominal or lumbar radiographic exams during the first trimester and compared them with 527 unexposed pregnancies (Choi et al., 2013). Consistent with the results of our study, this Korean study observed no significant associations between having a radiographic exam of the pelvis, lumbar spine, or abdomen during the periconceptional period.

Our study has some limitations. Despite the very large overall sample size of this study, our statistical power remains low to assess pelvic or fetal exposure to IR from radiographic exams, because only 0.9% of women reported these types of exposures. We used self-reported information, which asked mothers to recall radiologic exam history. Thus, our results may be subject to recall bias. As the NBDPS database does not include single-gene disorders or chromosomal abnormalities, we were not able to assess the association between maternal exposure to IR and these types of disorders. Also, estimates of gestational age at the time of these exposures were calculated from the mother’s report of her estimated day of delivery and the infant’s date of birth. For most U.S. women, estimates of this type will incorporate results of early ultrasound exams. Nonetheless, it is likely that some nondifferential misclassification of the gestational age at the time of the radiologic exams is present in this study.

As the NBDPS database includes data on maternal exposures to many different potential risk factors during the periconceptional period, we were able to limit the possibility for confounding by a variety of factors, including whether mothers had injury during pregnancy and BMI. Unfortunately, we did not have any information on the symptoms that elicited the radiologic exams in this study or the conditions that were diagnosed by the exams. The majority of conventional x-rays and CT scans of the lumbar spine are ordered to evaluate low back pain which is a very common condition that occurs among women of all age groups. Conventional x-rays and CT scans of the abdomen and pelvis are most commonly ordered to evaluate the possibility of appendicitis, ovarian cysts, or kidney stones. As we did not have information on these conditions, we could not evaluate the possibility that one or more of these conditions might be a cause of birth defects rather than the radiologic procedure that was used to diagnose it.

We could have estimated the fetal or gonadal dose of IR for each mother in the study based on published estimates of fetal doses for different types of radiologic exams. However, as we do not know how many scans were taken for each procedure, how long they were exposed to fluoroscopy, and what type or dose of radiotracers were used for nuclear medicine studies, such an approach might have suggested that our study had more precision that it actually does. Therefore, we used a qualitative approach, only assessing exposure to radiologic exams that were directed at the pelvis or the entire body. In Table 3, we present results that are stratified by radiologic exams associated with different average fetal doses of IR. Future studies need to measure maternal exposure to radiologic exams using medical records and conduct more refined dose-response assessments. They should also measure exposure to levels of naturally occurring IR and include birth defects caused by single-gene disorders and chromosomal abnormalities (Agency for Toxic and Disease, National Council on Radiation and Measurements, 2012).

Conclusions

Overall, we observed no association between maternal reports of exposure to IR and all birth defects in aggregate and the number of elevated ORs that we observed for specific types of birth defects is consistent with the number of elevated ORs that would be expected due to statistical fluctuation. This is consistent with the fact that the levels of IR associated with radiographic exams in the United States are not thought to be associated with harmful health effects to pregnant women or their fetuses. Although, 2 of 19 ORs for specific categories of birth defects were significantly elevated, these results should be interpreted cautiously, because they are based on maternal report and based on small number of exposed cases. The results of this study are likely to be useful for generating hypotheses for further studies of exposure to IR. A large study linking existing medical records to records of birth defects could potentially be conducted and would provide more accurate measurements of the type of radiologic exams that mothers are exposed to and timing of those exams during gestation.

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TABLE 1

Demographic Characteristics among Mothers in the National Birth Defects Prevention Study, 1997 to 2009

	Case (*N* = 27535)		Control (*N* = 10108)		
	n	**%**	***n***	**%**	**Crude OR (95% CI)**
Maternal age at delivery (yrs)					
< 18	984	3.57	357	3.53	1.05 (0.92, 1.20)
18 – 24	8424	30.59	3002	29.70	1.07 (1.00, 1.13)
25 – 29	7357	26.72	2792	27.62	1.0
30 – 34	6634	24.09	2560	25.33	0.98 (0.92, 1.05)
35 – 39	3341	12.13	1172	11.59	1.08 (1.00, 1.17)
≥ 40	795	2.89	225	2.23	1.34 (1.15, 1.56)
Maternal race/ethnicity					
Non-Hispanic white	16148	59.00	5875	58.63	1.00
Non-Hispanic black	2792	10.20	1115	11.13	0.91 (0.85, 0.98)
Hispanic, born in U.S.	2775	10.14	960	9.58	1.05 (0.97, 1.14)
Hispanic, born out of U.S.	3696	13.50	1349	13.46	1.00 (0.93, 1.07)
Other	1960	7.16	721	7.20	0.99 (0.90, 1.08)
Maternal education (yrs)					
0–8	1553	5.74	520	5.24	1.02 (0.91, 1.14)
9 – 11	3328	12.30	1163	11.73	0.98 (0.90, 1.06)
12	7023	25.95	2394	24.14	1.0
13 – 15	7405	27.36	2684	27.06	0.94 (0.88, 1.00)

	Case (*N* = 27535)		Control (*N* = 10108)		
	n	**%**	***n***	**%**	**Crude OR (95% CI)**
≥ 16	7758	28.66	3157	31.83	0.84 (0.79, 0.89)
Prepregnancy BMI (kg/m^2)					
Underweight (< 18.5)	1461	5.56	523	5.41	1.09 (0.98, 1.21)
Normal weight (18.5 – 24.9)	13467	51.21	5236	54.12	1.0
Overweight (25 – 30)	6056	23.03	2210	22.84	1.07 (1.01, 1.13)
Obese (≥ 30)	5316	20.21	1705	17.62	1.21 (1.14, 1.30)
Household income ($)					
< 10,000	4962	19.57	1699	18.56	1.02 (0.96, 1.09)
10,000 ≤ income < 50,000	11924	47.03	4175	45.60	1.0
≥ 50,000	8467	33.40	3281	35.84	0.90 (0.86, 0.95)
Any consumption of alcohol[b]					
Yes	9706	35.93	3638	36.73	0.97 (0.92, 1.01)
No	17305	64.07	6266	63.27	1.0
Preexisting diabetes					
Yes	581	2.11	57	0.56	3.80 (2.89, 4.99)
No	26920	97.89	10038	99.44	1.0
Use of supplements containing folic acid[c]					
Daily use	6762	24.63	2605	25.84	0.94 (0.89, 0.99)
Any use	7133	25.98	2570	25.49	1.00 (0.95, 1.06)
No use	13561	49.39	4907	48.67	1.00

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	Case (*N* = 27535)		Control (*N* = 10108)		
	n	**%**	***n***	**%**	**Crude OR (95% CI)**
Any smoking[d]					
Yes	5598	20.63	1813	18.22	1.17 (1.10, 1.24)
No	21538	79.37	8140	81.78	1.0
Illicit drug use[e]					
Yes	1593	5.87	514	5.17	1.15 (1.03, 1.27)
No	25528	94.13	9430	94.83	1.0
First live birth					
Yes	11752	42.75	4017	39.78	1.13 (1.08, 1.18)
No	15736	57.25	6081	60.22	1.0
Study site					
Arkansas	3674	13.34	1275	12.61	1.0
California	3585	13.02	1146	11.34	1.09 (0.99, 1.19)
Iowa	2564	9.31	1118	11.06	0.80 (0.72, 0.88)
Massachusetts	3416	12.41	1187	11.74	1.00 (0.91, 1.10)
New Jersey	1625	5.90	577	5.71	0.98 (0.87, 1.10)
New York	1853	6.73	854	8.45	0.75 (0.68, 0.84)
Texas	3150	11.44	1231	12.18	0.89 (0.81, 0.97)
CDC/Atlanta	3140	11.40	1059	10.48	1.03 (0.94, 1.13)
North Carolina	1880	6.83	803	7.94	0.81 (0.73, 0.90)

	Case (*N* = 27535)		Control (*N* = 10108)		
	n	**%**	***n***	**%**	**Crude OR (95% CI)**
Utah	2648	9.62	858	8.49	1.07 (0.97, 1.18)
Injury[e]					
Yes	2468	8.97	814	8.06	1.12 (1.04, 1.22)
No	25060	91.03	9291	91.94	1.0
Maternal exposure to radiographic exams of the urinary tract, lumbar spine, abdomen or pelvis, during the critical period[a]					
Exposed	220	0.92	73	0.83	1.11 (0.85, 1.45)
Unexposed	23716	99.08	8765	99.17	1.0

[a] Between 3 months prior to conception and the end of the first trimester of pregnancy.

[b] Any consumption of alcohol between first month of pregnancy and fourth month of pregnancy.

[c] Use of supplements containing folic acid between 1 month prior to conception and the end of the first month of pregnancy.

[d] Any smoking between 1 month prior to conception and the end of the first trimester of pregnancy.

[e] Between 3 months prior to conception and the date of delivery.

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TABLE 2

Odds Ratios for Associations between Maternal Exposure to Radiologic Exams of the Maternal Urinary Tract, Lumbar Spine, Abdomen, or Pelvis during the Periconceptional Period[a] and Isolated Birth Defects, National Birth Defects Prevention Study, 1997 to 2009

	From 3 months before conception to conception			From conception to 3 months after conception	
	Unexposed[b]	Exposed[c]	AOR[d]	Exposed[c]	AOR[d]
	(*N*)	(*N*)	(95% CI[e])	(N)	(95% CI[e])
All birth defects in aggregate					
Controls	7644	45		24	
Case	20939	130	1.03 (0.73, 1.45)	75	1.06 (0.67, 1.68)
Broad group of birth defects					
Neural tube defects[g]	1217	2	0.27[f] (0.07, 1.12)	3	0.66[f] (0.20, 2.16)
Other central nervous system defects[h]	397	3	1.28[f] (0.40, 4.13)	4	2.74[f] (0.96, 7.84)
Oral clefts[ij]	2685	15	0.85 (0.47, 1.54)	8	0.86 (0.38, 1.93)
Gastrointestinal defects[k]	1011	4	0.68[f] (0.24, 1.89)	5	1.62 (0.61, 4.29)
Genitourinary defects[l]	1683	7	0.69 (0.31, 1.56)	5	1.04 (0.38, 2.85)
Musculoskeletal[m]	2351	15	1.05 (0.58, 1.90)	6	0.85 (0.34, 2.10)
Conotruncal defects[n]	1462	6	0.68 (0.29, 1.62)	9	2.12 (0.98, 4.60)
LVOT defects[o]	1293	10	1.14 (0.57, 2.29)	8	1.74 (0.77, 3.95)
RVOT defects[p]	1245	9	1.08 (0.52, 2.25)	-	-
Septal defects[q]	2750	24	1.42 (0.85, 2.37)	8	0.81 (0.36, 1.84)
Isolated birth defects					

	From 3 months before conception to conception			From conception to 3 months after conception	
	Unexposed[b]	Exposed[c]	AOR[d]	Exposed[c]	AOR[d]
	(*N*)	(*N*)	(95% CI[e])	(N)	(95% CI[e])
Spina bifida	732	-	-	2	0.72[f] (0.17, 3.03)
Dandy - Walker malformation	67	-	-	2	7.73[f] (1.81, 33.0)
Hydrocephaly	239	2	1.44[f] (0.35, 5.94)	-	-
Anotia/microtia	275	3	1.70[f] (0.53, 5.49)	2	1.82[f] (0.43, 7.67)
Cleft palate w/o cleft lip[i]	872	8	1.38 (0.64, 2.96)	4	1.28[f] (0.45, 3.64)
Cleft lip w/wo cleft palate[i]	1813	7	0.59 (0.26, 1.32)	4	0.76[f] (0.29, 1.96)
Esophageal atresia	203	3	2.54[f] (0.78, 8.24)	-	-
Hypospadias	1528	7	0.74 (0.31, 1.78)	4	0.67[f] (0.22, 2.01)
Limb defects[l]	593	4	1.15[f] (0.41, 3.22)	4	1.86[f] (0.65, 5.30)
Craniosynostosis	960	2	1.14[f] (0.49, 2.68)	-	-
Single ventricle/complex heart	183	2	1.86[f] (0.45, 7.70)	-	-
Tetralogy of Fallot	655	3	0.81[f] (0.25, 2.61)	-	-
D-transposition of the great arteries	486	3	1.42[f] (0.51, 3.96)	5	3.85 (1.45, 10.3)
AVSD defects[r]	183	3	2.88[f] (0.89, 9.34)	-	-
Coarctation of the aorta	663	6	1.34 (0.56, 3.17)	5	2.23 (0.83, 6.02)
Pulmonary valve stenosis[s]	932	5	0.79 (0.30, 2.03)	-	-
VSD perimembranous	1047	7	1.02 (0.45, 2.30)	2	0.53[f] (0.13, 2.23)

	From 3 months before conception to conception			From conception to 3 months after conception	
	Unexposed[b]	Exposed[c]	AOR[d]	Exposed[c]	AOR[d]
	(*N*)	(*N*)	(95% CI[e])	(N)	(95% CI[e])
ASD secundum	1303	13	1.49 (0.78, 2.82)	4	0.85[f] (0.30, 2.44)
Complex cardiac defects	1141	9	1.19 (0.57, 2.48)	3	0.73[f] (0.22, 2.39)
Non-isolated birth defects[t]	3069	22	1.20 (0.72, 2.03)	11	1.07 (0.51, 2.23)

[a] Between 3 months prior to conception and the end of the first trimester of pregnancy.

[b] Includes mothers who were not exposed to radiologic exams between 3 months prior to conception and the end of the pregnancy.

[c] Includes mothers who were only exposed to radiologic exams in the period.

[d] Adjusted for study site, household income, preexisting diabetes, injury, any smoking, and maternal BMI.

[e] 95% confidence interval.

[f] Crude odds ratios if number of exposed cases is greater than 1 and less than 5.

[g] Includes anencephaly, spina bifida, and encephalocele.

[h] Includes hydrocephaly, Dandy-Walker malformation, cerebellar hypoplasia, and holoprosencephaly.

[i] Compared with 7577 (7532 unexposed, and 45 exposed) from 3 months before conception to conception. Compared with 7556 (7532 unexposed, and 24 exposed) from conception to conception 3 months after conception.

[j] Includes cleft palate alone, and cleft lip w/wo cleft palate.

[k] Includes esophageal atresia, intestinal atresia/stenosis, duodenal atresia/stenosis, colonic atresia/stenosis, anorectal atresia/stenosis, and biliary atresia/stenosis.

[l] Includes cloacal exstrophy, hypospadias, bladder exstrophy, or bilateral renal agenesis and hypoplasia.

[m] Includes craniosynostosis, diaphragmatic hernia, omphalocele, and gastroschisis,

[n] Includes truncus arteriosus, interrupted aortic arch (IAA) type B, IAA not otherwise specified (NOS), tetralogy of Fallot, d-transposition of the great arteries, double outlet right ventricle (DORV) with transposition of the great arteries (TGA), DORV-Other, and ventricular septal (VSD) conoventricular.

[o] Left ventricular outflow tract (LOVT) defects includes hypoplastic left heart syndrome, IAA type A, coarctation of the aorta, and aortic stenosis.

[p] Right ventricular outflow tract (RVOT) defects includes pulmonary atresia, pulmonary valve stenosis, Ebstein anomaly, and tricuspid atresia.

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[q] Includes VSD perimembranous, VSD muscular, VSD NOS, VSD ostium secundum (OS), multiple VSDs, and atrial septal defect (ASD) secundum.

[r] Atrioventricular septal defects (AVSD).

[s] Compared with 7371 (7326 unexposed, and 45 exposed) from 3 months before conception to conception. Compared with 7350 (7326 unexposed, and 24 exposed) from conception to conception 3 months after conception.

[t] Includes babies with had two or more major unrelated defects in different organ systems.

TABLE 3

Odds Ratios for Associations between Maternal Exposure to Radiologic Exams of the Urinary Tract, Lumbar Spine, Abdomen, or Pelvis and any NBDPS Birth Defects during the Periconceptional Period[a], Stratified by Type of Radiologic Exam: National Birth Defects Prevention Study, 1997 to 2009

Type of medical exams	3 months before conception to conception				Conception to 3 months after conception		
	Average fetal dose[a,f]	Case	Control		Case	Control	
	(mGy)	(*N*)	(*N*)	AOR[b] (95% CI[c])	(*N*)	(*N*)	AOR[b] (95% CI[c])
Nuclear medicine	1 – 19[i]	4	4	0.46[d] (0.12, 1.72)	4	1	1.11[d] (0.22, 5.50)
CT scan		26	10	0.98 (0.47, 2.03)	17	2	2.80 (0.64, 12.2)
CT-pelvis	10 – 25[j]	5	3	0.70 (0.17, 2.94)	4	-	-
CT-lumbar	2 – 20[j]	-	-	-	2	1	0.74[d] (0.07, 8.15)
CT-Abdomen	2–8[j]	20	6	1.22 (0.49, 3.04)	11	1	3.46 (0.44, 27.1)
HSG[g]	2.7 – 4.6[k]	7	2	1.43 (0.30, 6.89)	-	2	-
IVP or KUB[h]	6[l]	12	2	2.21 (0.49, 9.86)	10	3	1.28 (0.35, 4.66)
Conventional x-ray[e]	1 – 3.4[j]	74	24	1.09 (0.68, 1.73)	44	15	0.96 (0.53, 1.74)
Total body scan	10 – 15[m]	2	2	0.37[d] (0.05, 2.63)	-	-	-
More than one of radiologic exams		5	1	1.55 (0.18, 13.4)	-	-	-

[a] Between 3 months prior to conception and the end of the first trimester of pregnancy.

[b] Adjusted for study site, household income, preexisting diabetes, injury, any smoking, and maternal BMI.

[c] 95% confidence interval.

[d] Crude odds ratios if number of exposed cases is greater than 1 and less than 5 (1 < exposed cases <5).

[e] Conventional x-ray of pelvis, lumbar spine, or abdomen.

[f] The average level of IR delivered to the fetus.

[g] Hysterosalpingograms (HSG).

[h] Intravenous pyelogram (IVP) or kidneys, ureters, and bladder (KUB).

[i] Russell et al.,1997.

[j] Chen et al.,2008; International commission on radiological protection (ICRP),2000; Lowe,2004; Osei and Darko,2012.

[k] Fernandez et al., 1996; Roshan et al.,2003.

[l] Chen et al.,2008; McCollough et al.,2007.

[m] Angel et al.,2008.