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Nuclear Radiation and Prevalence of Structural Birth Defects among Infants Born to Women from the Marshall Islands

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Abstract

Background: With their unique history of exposure to extensive nuclear testing between 1946 and 1958, descendants of Marshall Island residents may have underappreciated genetic abnormalities, increasing their risk of birth defects.

Methods: We conducted a retrospective cohort study of resident women with at least one singleton live birth between 1997 and 2013 in northwest Arkansas using state birth certificate data linked to data from the Arkansas Reproductive Health Monitoring System, a statewide birth defects registry. We calculated unadjusted and adjusted prevalence ratios (PR) and 95% confidence intervals (CI) from modified Poisson regression analyses for non-Hispanic (NH) whites, NH-blacks, Hispanics and Marshallese, using NH-whites as the reference group.

Results: Of the 91,662 singleton births during the study period, 2,488 were to Marshallese women. Due to the relatively small number of Marshallese births, we could not calculate prevalence estimates for some defects. Marshallese infants had higher rates of congenital cataracts

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(PR=9.3; 95% CI: 3.1, 27.9). Although the number of defects was low, Marshallese infants also had higher rates of truncus arteriosus (PR=44.0; 95% CI: 2.2, 896.1).

Conclusions: Marshallese infants may have increased risk of specific birth defects, but estimates are unstable because of small sample size so results are inconclusive. Larger population-based studies would allow for further investigation of this potential risk among Marshallese infants.

Keywords

Marshall Islands; birth defects; nuclear radiation; Chernobyl; Hiroshima; Pacific Islander

INTRODUCTION

From 1947 to 1986, the Marshall Islands, a group of 29 atolls (1,200 islands) in the Pacific Ocean, were administratively controlled by the United States (U.S.) as a United Nations Trust Territory of the Pacific Islands(McElfish, Hallgren, & Yamada, 2015). Between 1946 and 1958, the U.S. military conducted extensive nuclear weapons testing in the Marshall Islands (Barker, 2012; S. Simon & Robison, 1997; S Yamada, Dodd, Soe, Chen, & Bauman, 2004). The 67 nuclear weapon devices detonated during this period are the combined equivalent to more than 108 megatons (7,200 Hiroshima-sized bombs) and exposed islanders to significant levels of nuclear radiation (Cronkite, Bond, & Conard, 1995; Lessard, Miltenberger, Cohn, Musolino, & Conard, 1984; N. Pollock, 2002; Robison et al., 1997; S. L. Simon, 1997). Inhabitants of the atolls used for direct nuclear testing were relocated; however, those living on nearby atolls were not relocated and received exposure to nuclear fallout (Barker, 2012; The U.S. Advisory Comittee on Human Radiation Experiments, 1995). The most significant exposure occurred due to miscalculations in wind direction in 1954 during Operation Castle's test of the 15 megaton hydrogen bomb, code named, "Bravo", the largest nuclear device ever denoted, resulting in acute exposure of inhabitants of nearby atolls to radiation and nuclear fallout (Reuther, 1997). Inhabitants of many atolls in the Marshall Islands had chronic exposure to radiation through ingestion of contaminated food and water (Johnston, 2009; S. L. Simon, Bouville, Melo, Beck, & Weinstock, 2010).

The U.S. government (i.e., Brookhaven National Laboratories) implemented ongoing medical surveillance, documented health effects and provided long-term medical care for the highly exposed Marshallese from specific atolls (Reuther, 1997; The U.S. Advisory Comittee on Human Radiation Experiments, 1995); however, only two epidemiologic studies were ever conducted (S. L. Simon, Bouville, Land, & Beck, 2010). The studies showed high incidence of abnormal thyroid function, frank disease, and thyroid cancer among the Marshallese due to radiation exposure (Hamilton, van Belle, & LoGerfo, 1987; Takahashi et al., 1997). But no comprehensive epidemiologic studies were conducted among the Marshallese to identify other types of cancers or serious illnesses that could result from nuclear radiation exposure. Small population size, sparse population data and inadequate data sources hampered epidemiological investigations (N. J. Pollock, 2002). Furthermore, government investigations did not assess reproductive outcomes among all Marshallese men and women, only women on specific atolls, (The U.S. Advisory Comittee on Human Radiation Experiments, 1995) despite widespread reports from Marshallese women and

midwives of higher numbers of miscarriages, stillbirths, “jellyfish or grape babies” (fetuses without bones and transparent skin), limb reduction defects, and anencephaly (Johnston, 2009; N. J. Pollock, 2002; Reuther, 1997; S. Yamada, 2004). Based on results from birth cohort studies in Hiroshima and Nagasaki (Jordan, 2016; Nakamura, 2006). Scientists asserted that radiation levels on atolls not directly used for nuclear testing were not high enough to cause adverse reproductive outcomes, including birth defects (Johnston, 2009; Reuther, 1997). Subsequent tribunal investigations finally included miscarriages, stillbirths and birth defects as consequences of nuclear radiation exposure among Marshallese women, even though data was very sparse and causality due to nuclear radiation exposure was difficult to establish (Johnston, 2009; N. J. Pollock, 2002; Reuther, 1997; S. Yamada, 2004).

Displacement from contaminated atolls, rising sea levels, and high unemployment in the Republic of the Marshall Islands was impetus for migration of Marshallese starting in the 1980’s to Hawaii and the continental US. Migration to the U.S. mainland has increased rapidly over the past 20 years, and Arkansas has the largest Marshallese population in the continental U.S (≥40,000 in the US and ≥12,000 in Arkansas) (McElfish, Hallgren, et al., 2015). Anecdotal reports by Arkansas clinicians of a high number of birth defects among infants born to immigrant women from the Marshall Islands, combined with their unique exposure history, prompted this investigation. We investigated whether or not infants born to Arkansas resident women who were born in the Marshall Islands had a higher prevalence of birth defects than non-Hispanic (NH) white infants in Arkansas.

METHODS

We conducted a retrospective cohort study using all resident mothers from Benton and Washington Counties, Arkansas (more than 95% of the Marshallese population in Arkansas reside in these counties), who had one or more singleton, live births between January 1, 1997, and December 31, 2013 (women born between 1959 and 1996 in the Marshall Islands and of childbearing age between 1997 and 2013). The Arkansas Department of Health, Health Statistics Branch linked state birth certificate data to data from the Arkansas Reproductive Health Monitoring System (ARHMS). ARHMS is a population-based, statewide surveillance system that uses active case ascertainment methods to monitor approximately 40,000 births annually for reproductive health outcomes, including birth defects. Specially trained abstractors with degrees in Health Information Management actively ascertain relevant information from medical records at 46 birthing facilities, including all delivering hospitals, the state’s only pediatric specialty-care hospital and associated clinics, and high-risk pregnancy and prenatal diagnosis centers. Eligibility for ARHMS includes live births with an initial diagnosis of major birth defects up to 2 years of age, stillbirths of at least 20 weeks’ gestation, early fetal losses, and elective terminations at any gestational age. ARHMS codes birth defects using the six-digit British Pediatric Association extension of the International Classification of Diseases, Ninth Edition Clinical Modification (ICD-9-CM) coding system, as modified by the Division of Birth Defects and Developmental Disabilities of the Centers for Disease Control and Prevention and by ARHMS. We excluded pregnancies ending in early fetal loss, elective termination or stillbirth from these analyses since we could not identify Pacific Islander subgroups from the

available data (e.g., records included maternal race/ethnicity but did not include maternal place of birth).

Study Variables

We extracted maternal socioeconomic and obstetric information from birth records: maternal age (<20, 20–29, 30–39, ≥40 years), maternal year of birth (1959–1969, 1970–1979, 1980–1989, and 1990–1996), education ((elementary (1–8 years of education), secondary (9–12 years), some college or higher (≥13 years)), marital status (married or unmarried), parity (1, 2 or ≥3 children), prenatal care, prenatal tobacco use, prenatal alcohol use and method of delivery. We classified maternal ethnicity (NH-white, NH-black, Hispanic, and Marshallese) based on birth records. We categorized women as Marshallese if the birth certificate designated the maternal race as Pacific Islander and the place of birth as the Republic of the Marshall Islands. We extracted data on infant outcomes from birth records: infant sex, birthweight (<1500, 1500–2499, 2500–4000 and >4000 grams), and gestational age (20–36, ≥37 completed weeks of gestation).

Statistical analyses

We calculated summary statistics for each study variable, expressed as means (standard deviation) for continuous variables and counts (percentage) for categorical variables. Prevalence-at-live birth for selected birth defects was calculated as the number of birth defects in the category divided by the number of live births for the racial/ethnic group multiplied by 10,000. Therefore, representation of the same infant may occur in more than one defect category. We determined crude prevalence ratios (PR) and 95% confidence intervals (CI) using NH white as the reference group. Adjusting for maternal age, education, marital status and parity in multivariable modified Poisson regression analyses, we calculated adjusted PRs and 95% CIs. To comply with ARHMS data suppression rules, which preserve patient confidentiality, we do not report results for categories that had < 5 cases. Statistical significance was set at $P<0.05$ or if the confidence interval excluded the null value. We performed all statistical analyses with SAS 9.4 software (SAS Inc., Cary, NC).

We conducted the research in accordance with the prevailing ethical principles. The Institutional Review Board at the University of Arkansas for Medical Sciences deemed the project exempt; the Arkansas Department of Health, Science Advisory Committee reviewed and approved the project protocol.

RESULTS

During the study period, fifteen percent of Arkansas births (n=99,045) were to women residing in Benton and Washington Counties. Of the births in those counties, 7,423 live births were excluded because they did not meet the study criteria (2,741 were not singletons and maternal ethnicity of 4,682 births did not fit the study categories or were missing); thus 91,622 singleton infants are in our study (Table 1). In both counties combined, Marshallese women had 2,488 (2.6%) singleton births. As displayed in Tables 1, the majority of Marshallese women only had 9 to 12 years of education, were unmarried, and had three or

more children. Only 52% of Marshallese women received prenatal care in the first trimester whereas 73% of Hispanic women and more than 80% of NH black and NH white women received prenatal care in the first trimester. Fifteen percent of Marshallese women received no prenatal care.

Overall, we did not observe higher rates of birth defects among Marshallese infants; 2.6% of NH white infants were born with birth defects whereas 2.3% of NH black, 2.1% of Hispanic and 2.2% of Marshallese infants were born with birth defects (Table 1). Prevalence estimates could not be calculated for many specific birth defect phenotypes due to the relatively small number of Marshallese and NH black births. Nevertheless, we did observe higher prevalence estimates for a few specific birth defect phenotypes among Marshallese infants (Table 2). Table 3 presents prevalence ratios. In unadjusted analyses, Marshallese infants more likely to have holoprosencephaly than NH white infants, but the increase was not statistically significant after adjusting potential confounders (PR=9.3; 95% CI: 0.4, 206.1).

Among ophthalmic defects, Marshallese infants had a higher occurrence of congenital cataracts than NH white infants did (PR=9.3; 95% CI: 3.1, 27.9) after adjusting for covariates. For selected cardiovascular defects, Marshallese infants were more likely to have common truncus (PR=44.0; 95% CI: 2.2, 896.1) compared to NH whites. Marshallese infants were also more likely to have pulmonary valve atresia/stenosis, hypoplastic left heart syndrome, total anomalous pulmonary venous return, and double outlet right ventricle; but none of the estimates were statistically significant.

To further test our hypothesis, we assessed whether Marshallese women born in the 1954–1969 decade had a higher prevalence overall among their children compared to NH white women born in the same decade and found that they had a 2.4 fold higher prevalence, but it was not statistically significant (95% CI: 0.9, 6.5). After adjusting for covariates, the prevalence ratio decreased to 1.5 and remained not statistically significant (95% CI: 0.5, 4.7). Marshallese women born in the other decades did not have higher prevalence of birth defects overall among their children compared to NH white women (data not shown).

DISCUSSION

This study assessed whether or not Marshallese infants had higher rates of birth defects overall or for specific defect phenotypes. Our results show that Marshallese infants had a higher occurrence of congenital cataracts, and truncus arteriosus. Several other defects had higher prevalence ratios but were not statistically significant. Thus, based on these results, it is unclear what the true pattern of association is in the Marshallese population.

At the time of weapons testing in the Marshall Islands, scientists believed that exposure to nuclear radiation did not increase the risk of birth defects. However, since 1945, four major events provided opportunity to examine nuclear radiation exposure and subsequent risk of birth defects in offspring. Results from epidemiologic studies are inconsistent. Between 1948 and 1954, the Atomic Bomb Casualty Commission and the Radiation Effects Research Foundation conducted prospective cohort studies to investigate the risk of birth defects in offspring of women exposed to nuclear radiation during the atomic bombings of Hiroshima

and Nagasaki, Japan. Investigators found higher rates of growth deficiencies, intellectual impairments, and neurologic deficits, but no increased risk of birth defects (Jordan, 2016; Nakamura, 2006). Numerous studies investigated risk of birth defects after exposure to nuclear radiation from the nuclear power plant explosion in Chernobyl, Ukraine, in 1986. The results of these studies varied significantly. Several studies reported no change in rates of birth defects, while others reported higher rates of congenital anomalies. Despite the same exposing event, studies reported increased rates of different congenital anomalies, depending on the geographic region. For example, there were higher rates of multiple congenital malformations, trisomy 21, polydactyly and reduction limb defects in Belarus and regions of Germany; while in Croatia and Turkey they were higher rates of central nervous and neural tube defects (Akar, Cavdar, & Arcasoy, 1988; Caglayan, Kayhan, Mentesoglu, & Aksit, 1989; Dolk & Nichols, 1999; Feshchenko, Schroder, Muller, & Lazjuk, 2002; Guvenc et al., 1993; Haeusler, Berghold, Schoell, Hofer, & Schaffer, 1992; Harjulehto-Mervaala, Salonen, Aro, & Saxen, 1992; Harjulehto, Aro, Rita, Rytomaa, & Saxen, 1989; Hoffmann, 2001; Irl, Schoetzau, van Santen, & Grosche, 1995; Kruslin, Jukic, Kos, Simic, & Cviko, 1998; Lazjuk, Nikolaev, & Novikova, 1997; Lie et al., 1992; Little, 1993; Mocan, Aydemir, Bozkaya, Mocan, & Ozbay, 1992; Mocan, Bozkaya, Mocan, & Furtun, 1990; Sperling, Neitzel, & Scherb, 2012). The Polissia regions of the Ukraine reported higher rates of microcephaly, neural tube defects, and microphthalmia (W. Wertelecki et al., 2017; Wladimir Wertelecki et al., 2016; W. Wertelecki et al., 2018). In contrast to Chernobyl, studies from the 2011 Fukushima Daiichi Nuclear Power Plant disaster in Japan, showed no statistically significant differences in birth defect prevalence between exposed and unexposed areas of Japan (Fujimori et al., 2014).

Strengths and Limitations

This study exemplifies the challenges of investigating rare health outcomes (increased risk or higher prevalence of specific birth defect phenotypes) in populations with low birth rates or small population sizes overall. Although this study has the largest population of infants born to Marshallese immigrant women to date, we still had an insufficient number of cases of birth defects to calculate prevalence for many specific phenotypes. Although the Marshallese population has a history of exposure to nuclear radiation, we did not have information on exposure status among the women. Women in our study were born between 1959 and 1996 and those born between 1959 and the 1970’s would have been exposed to nuclear radiation in utero and/or as children exposed to contaminated soil, food and water. Moreover, exposure to nuclear radiation was heterogeneous among the Marshall Islands, with some atolls receiving more exposure than others; we have no information on which specific atoll in the Marshall Islands women were born or lived before immigrating to the US. Even with a history of nuclear radiation exposure, it is difficult to attribute any increased rate of birth defects observed among Marshallese infants to a specific exposure, especially one occurring in utero or during childhood. Since the introduction of Western foods into the Marshall Islander diet after World War II, native and expatriate Marshallese women have high rates of pre-pregnancy obesity and diabetes (Center for Disease Control and Prevention, 2011; Ichiho, deBrum, Kedi, Langidrik, & Aitaoto, 2013; McElfish, Bridges, et al., 2015; Minegishi et al., 2007; S Yamada et al., 2004) which are known risk factors for structural birth defects (Casson et al., 1997; Kallen, 1998; Shaw, Nelson, & Moore, 2002; Shaw, Velie,

& Schaffer, 1996; Towner et al., 1995; Waller et al., 1994; Watkins, Scanlon, Mulinare, & Khoury, 1996). Another limitation is that if birth certificates did not indicate the Marshall Islands as the maternal place of birth, we would be unable to ascertain all birth defect cases that occurred to Marshallese women. Despite these limitations, our study has several strengths, which include a large population of births to immigrant women from the Marshall Islands; ascertainment of cases of birth defects from an active statewide, population-based, birth defects surveillance system; and a multi-ethnic study population.

The older and middle-aged Marshallese immigrant population in the U.S. has a unique history of exposure to nuclear radiation during fetal development and childhood. Although it remains unclear if they have a higher rate of birth defects in offspring compared to NH-whites, the current scientific literature suggests that it is plausible. Further exploration of this possible association requires additional research including evaluation of other maternal risk factors.

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Table 1.

Sociodemographic Characteristics of NH White, NH Black, Hispanic and Marshallese Mothers Benton and Washington Counties, Arkansas, 1997–2013 (n=91,622)

	NH[a] White (n=65,800)		NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)		
	n	%	n	%	n	%	n	%	P[b]
Maternal age									<0.01
<20 years	7,081	10.8	220	13.1	2,946	13.6	220	8.9	
20–29 years	38,335	58.3	981	58.4	12,209	56.4	1,675	67.4	
30–39 years	19,368	29.4	454	27.0	6,032	27.9	581	23.4	
≥40 years	1,000	1.5	25	1.5	461	2.1	11	0.4	
Maternal Decade of Birth									<.0001
1954 – 1969	8,044	12.2	130	7.7	1,946	9.0	66	2.7	
1970 – 1979	28,404	43.2	629	37.5	8,853	40.9	794	31.9	
1980 – 1989	26,023	39.6	760	45.3	9,252	42.7	1,415	56.9	
1990 – 1999	3,294	5.0	160	9.5	1,596	7.4	212	8.5	
Maternal Education									<0.01
Elementary (1–8 years)	697	1.1	6	0.4	6,591	31.5	149	6.5	
Secondary (9–12 years)	31,111	47.6	672	40.8	11,763	56.2	1,978	85.7	
Some college or higher (≥13 years)	33,594	51.4	969	58.8	2,572	12.3	180	7.8	
Marital Status									<0.01
Married	48,689	74.0	788	46.9	12,517	57.8	781	31.4	
Unmarried	17,068	26.0	892	53.1	9,133	42.2	1,706	68.6	
Parity									<0.01
1 child	28,524	43.4	745	44.4	7,215	33.4	562	22.7	
2 children	20,161	30.7	467	27.9	6,007	27.8	503	20.3	
≥3 children	16,997	25.9	465	27.7	8,382	38.8	1,414	57.0	
Prenatal care									
Prenatal care in the 1st trimester	58,522	87.4	1,433	83.4	15,835	73.2	1,262	52.2	<0.01
No prenatal care	840	1.3	57	3.4	524	2.4	480	19.3	<0.01
Birth defects	1697	2.6	39	2.3	459	2.1	54	2.2	0.21

[a] NH=Non-Hispanic

[b] Comparison between Non-Hispanic White and Marshallese.

Table 2.

Prevalence (per 10,000 Live Births) and 95% confidence intervals for Birth Defects among Liveborn Infants by Maternal Race/Ethnicity, Benton and Washington Counties, Arkansas, 1997–2013.

	NH[a] White (n=65,800)		NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)	
	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]
Central Nervous System								
Anencephaly	6	0.9 (0.3, 2.0)	0	-	≤4[c]	0.9 (0.1, 3.3)	0	-
Spina bifida without anencephaly	26	4.0 (2.6, 5.8)	≤4[c]	5.9 (0.2, 33.1)	11	5.1 (2.5, 9.1)	≤4[c]	4.0 (0.1, 22.4)
Hydrocephaly without spina bifida	43	6.5 (4.7, 8.8)	0	-	15	6.9 (3.9, 11.4)	≤4[c]	4.0 (0.1, 22.4)
Microcephaly	23	3.5 (2.2, 5.2)	0	-	6	2.8 (1.0, 6.0)	≤4[c]	16.1 (4.4, 41.1)
Holoprosencephaly	≤4[c]	0.5 (0.1, 1.3)	0	-	≤4[c]	0.5 (0.0, 2.6)	≤4[c]	8.0 (1.0, 29.0)
Subtotal	*100*	15.2 (12.4, 18.5)	≤4[c]	*6 (0.2, 33.1)*	*32*	*14.8 (10.1, 20.9)*	*8*	*32.2 (13.9, 63.3)*
Eye								
Anophthalmia/microphthalmia	16	2.4 (1.4, 3.9)	0	-	≤4[c]	1.8 (0.5, 4.7)	≤4[c]	4.0 (0.1, 22.4)
Congenital cataract	15	2.3 (1.3, 3.8)	0	-	≤4[c]	1.8 (0.5, 4.7)	≤4[c]	16.1 (4.4, 41.1)
Subtotal	*30*	*4.6 (3.1, 6.5)*	*0*	-	*8*	*3.7 (1.6, 7.3)*	*5*	*20.1 (6.5, 46.8)*
Ear								
Anotia/microtia	9	1.4 (0.6, 2.6)	0	-	8	3.7 (1.6, 7.3)	0	-
Cardiovascular								
Truncus arteriosus	≤4[c]	0.3 (0, 1.1)	≤4[c]	6 (0.2, 33.1)	≤4[c]	0.5 (0.0, 2.6)	≤4[c]	4.0 (0.1, 22.4)
Transposition of the great arteries	34	5.2 (3.6, 7.2)	0	-	≤4[c]	1.8 (0.5, 4.7)	0	-
Tetralogy of Fallot	19	2.9 (1.7, 4.5)	0	-	9	4.2 (1.9, 7.9)	0	-
Ventricular septal defect	378	57.4 (51.8, 63.5)	8	47.6 (20.6, 93.6)	115	53.1 (43.9, 63.7)	10	40.2 (19.3, 73.8)
Atrial septal defect	211	32.1 (27.9, 36.7)	≤4[c]	17.9 (3.7, 52.1)	62	28.6 (22.0, 36.7)	11	44.2 (22.1, 79.0)
Atrioventricular septal defect	44	6.7 (4.9, 9.0)	≤4[c]	6 (0.2, 33.1)	8	3.7 (1.6, 7.3)	≤4[c]	8.0 (1.0, 29.0)
Pulmonary valve atresia and stenosis	80	12.2 (9.6, 15.1)	≤4[c]	23.8 (6.5, 60.8)	23	10.6 (6.7, 15.9)	6	24.1 (8.9, 52.4)

	NH[a] White (n=65,800)		NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)	
	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]
Tricuspid valve atresia and stenosis	7	1.1 (0.4, 2.2)	0	-	≤4[c]	1.4 (0.3, 4.0)	0	-
Ebstein anomaly	9	1.4 (0.6, 2.6)	0	-	≤4[c]	1.8 (0.5, 4.7)	0	-
Aortic valve stenosis	18	2.7 (1.6, 4.3)	0	-	8	3.7 (1.6, 7.3)	0	-
Hypoplastic left heart syndrome	18	2.7 (1.6, 4.3)	0	-	≤4[c]	1.4 (0.3, 4.0)	≤4[c]	4.0 (0.1, 22.4)
Patent ductus arteriosus	140	21.3 (17.9, 25.1)	11	65.5 (32.7, 116.9)	41	18.9 (13.6, 25.7)	≤4[c]	16.1 (4.4, 41.1)
Coarctation of the aorta	49	7.4 (5.5, 9.8)	0	-	12	5.5 (2.9, 9.7)	≤4[c]	4.0 (0.1, 22.4)
Total anomalous pulmonary venous connection	≤4[c]	0.6 (0.2, 1.6)	0	-	≤4[c]	0.5 (0.0, 2.6)	≤4[c]	8.0 (1.0, 29.0)
Interrupted aortic arch	7	1.1 (0.4, 2.2)	0	-	0	-	0	-
Double outlet right ventricle	11	1.7 (0.8, 3.0)	≤4[c]	6.0 (0.2, 33.1)	5	2.3 (0.7, 5.4)	≤4[c]	8.0 (1.0, 29.0)
Subtotal	*765*	*116.3 (108.2, 124.7)*	*22*	*131 (82.2, 197.6)*	*220*	*101.6 (88.7, 15.9)*	*28*	*112.5 (74.9, 162.2)*
Orofacial								
Cleft palate alone	35	5.3 (3.7, 7.4)	0	-	15	6.9 (3.9, 11.4)	≤4[c]	8.0 (1.0, 29.0)
Cleft lip alone	26	4.0 (2.6, 5.8)	0	-	≤4[c]	1.4 (0.3, 4.0)	0	-
Cleft lip with cleft palate	36	5.5 (3.8, 7.6)	0	-	14	6.5 (3.5, 10.8)	0	-
Subtotal	*92*	*14.0 (11.3, 17.1)*	*0*	-	*31*	*14.3 (9.7, 20.3)*	≤4[c]	*8.0 (1.0, 29.0)*
Gastrointestinal								
Esophageal atresia/tracheoesophageal fistula	25	3.8 (2.5, 5.6)	0	-	≤4[c]	1.4 (0.3, 4.0)	0	-
Rectal and large intestinal atresia/stenosis	30	4.6 (3.1, 6.5)	≤4[c]	17.9 (3.7, 52.1)	8	3.7 (1.6, 7.3)	≤4[c]	4.0 (0.1, 22.4)
Pyloric stenosis	113	17.2 (14.2, 20.6)	≤4[c]	6.0 (0.2, 33.1)	43	19.9 (14.4, 26.7)	0	-
Hirshsprung's disease	18	2.7 (1.6, 4.3)	0	-	≤4[c]	0.5 (0.0, 2.6)	≤4[c]	4.0 (0.1, 22.4)
Small intestinal atresia/stenosis	22	3.3 (2.1, 5.1)	0	-	≤4[c]	1.8 (0.5, 4.7)	≤4[c]	4.0 (0.1, 22.4)
Subtotal	*211*	*32.1 (27.9, 36.7)*	≤4[c]	*23.8 (6.5, 60.8)*	*60*	*27.7 (21.2, 35.7)*	≤4[c]	*16.1 (4.4, 41.1)*
Genitourinary								
Renal agenesis/hypoplasia	20	3.0 (1.9, 4.7)	0	-	8	3.7 (1.6, 7.3)	0	-

	NH[a] White (n=65,800)		NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)	
	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]	Cases	Prev (95% CI)[b]
Obstructive genitourinary defect	116	17.6 (14.6, 21.1)	≤4[c]	23.8 (6.5, 60.8)	29	13.4 (9.0, 19.2)	≤4[c]	16.1 (4.4, 41.1)
Hypospadias	284	84.2 (38.3, 48.5)	7	82.7 (16.8, 85.7)	25	22.9 (7.5, 17)	5	39.8 (6.5, 46.8)
Cystic kidney	15	2.3 (1.3, 3.8)	0	-	5	2.3 (0.7, 5.4)	0	-
Subtotal	*420*	*63.8 (57.9, 70.2)*	*11*	*65.5 (32.7, 116.9)*	*67*	*30.9 (24, 39.3)*	*9*	*36.2 (16.6, 68.6)*
Musculoskeletal								
Limb deficiencies	27	4.1 (2.7, 6.0)	≤4[c]	6 (0.2, 33.1)	12	5.5 (2.9, 9.7)	≤4[c]	8.0 (1.0, 29.0)
Gastroschisis	43	6.5 (4.7, 8.8)	0	-	7	3.2 (1.3, 6.7)	0	-
Omphalocele	14	2.1 (1.2, 3.6)	0	-	6	2.8 (1.0, 6.0)	0	-
Congenital hip dislocation	12	1.8 (0.9, 3.2)	0	-	5	2.3 (0.7, 5.4)	≤4[c]	4.0 (0.1, 22.4)
Diaphragmatic hernia	26	4.0 (2.6, 5.8)	≤4[c]	17.9 (3.7, 52.1)	≤4[c]	1.4 (0.3, 4.0)	0	-
Craniosynostosis	52	7.9 (5.9, 10.4)	≤4[c]	6.0 (0.2, 33.1)	13	6.0 (3.2, 10.3)	0	-
Clubfoot	91	13.8 (11.1, 17)	≤4[c]	11.9 (1.4, 42.9)	26	12 (7.8, 17.6)	≤4[c]	8.0 (1.0, 29.0)
Prune belly	≤4[c]	0.2 (0.0, 0.8)	0	-	0	-	0	-
Subtotal	*257*	*39.1 (34.4, 44.1)*	*6*	*35.7 (13.1, 77.6)*	*72*	*33.3 (26.0, 41.9)*	≤4[c]	*16.1 (4.4, 41.1)*
Chromosomal								
Trisomy 13	≤4[c]	0.2 (0.0, 0.8)	0	-	≤4[c]	0.5 (0.0, 2.6)	0	-
Trisomy 18	15	2.3 (1.3, 3.8)	0	-	10	4.6 (2.2, 8.5)	≤4[c]	4.0 (0.1, 22.4)
Trisomy 21	74	11.2 (8.8, 14.1)	≤4[c]	6.0 (0.2, 33.1)	43	19.9 (14.4, 26.7)	≤4[c]	12.1 (2.5, 35.2)
Turner syndrome	≤4[c]	0.5 (0.1, 1.3)	0	-	≤4[c]	0.5 (0.0, 2.6)	0	-
Subtotal	*96*	*14.6 (11.8, 17.8)*	≤4[c]	*11.9 (1.4, 42.9)*	*56*	*25.9 (19.5, 33.6)*	*4*	*16.1 (4.4, 41.1)*
Other								
Achondroplastic dwarfism	≤4[c]	0.6 (0.2, 1.6)	0	-	≤4[c]	0.5 (0.0, 2.6)	≤4[c]	4.0 (0.1, 22.4)
Lung agenesis or aplasia	≤4[c]	0.2 (0.0, 0.8)	0	-	0	-	0	-
Total births with defects	1697	258.2 (246.2, 70.6)	39	232.1 (165.6,316)	459	212 (193.2,232.0)	54	217 (163.5, 282.3)

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[a] NH=Non-Hispanic;

[b] Prev (95% CI)= prevalence and 95% confidence intervals

[c] Data suppressed due to small numbers

Table 3.

Prevalence Ratios and 95% Confidence Intervals (CI) for Birth Defects among Liveborn Infants by Maternal race/Ethnicity in Benton and Washington Counties, Arkansas, 1997–2013

	NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)	
	PR[b] (95% CI)	PR[bc] (95% CI)	PR[b] (95% CI)	PR[bc] (95% CI)	PR[b] (95% CI)	PR[bc] (95% CI)
Central Nervous System						
Anencephaly	-	-	1.2 (0.3, 4.4)	1.1 (0.2, 6.9)	-	-
Spina bifida without anencephaly	1.5 (0.2, 11.2)	1.6 (0.2, 12.2)	1.3 (0.6, 2.7)	1.1 (0.5, 2.7)	1.1 (0.2, 8.1)	1.0 (0.2, 5.5)
Hydrocephaly without spina bifida	,	-	1.0 (0.6, 1.8)	1.0 (0.5, 2.1)	0.6 (0.1, 4.4)	0.6 (0.1, 4.8)
Holoprosencephaly	-	-	1.0 (0.1, 0.1)	0.6 (0.0, 8.6)	**18.8 (3.1, 115.3)**	9.3 (0.4, 206.1)
Subtotal	*0.4 (0.1, 2.8)*	*0.3 (0.1, 2.5)*	*1.0 (0.7, 1.5)*	*0.9 (0.5, 1.4)*	*2.0 (0.9, 4.2)*	*1.4 (0.6, 3.4)*
Eye						
Anophthalmia/microphthalmia	-	-	0.8 (0.3, 2.3)	0.6 (0.2, 1.9)	1.8 (0.2, 13.4)	1.0 (0.2, 6.9)
Congenital cataract	-	-	0.8 (0.3, 2.3)	0.7 (0.2, 2.2)	**7.1 (2.4, 21.3)**	**9.3 (3.1, 27.9)**
Subtotal	-	-	*0.9 (0.4, 1.9)*	*0.7 (0.3, 1.5)*	*4.9 (1.9, 12.6)*	*4.1 (1.5, 11.3)*
Ear						
Anotia/microtia	-	-	2.5 (1.0, 6.2)	2.0 (0.7, 5.4)	-	-
Cardiovascular						
Truncus arteriosus	**19.8 (1.8, 223.4)**	**18.8 (2.7, 130.7)**	1.5 (0.1, 7.4)	3.4 (0.2, 63.0)	**14.1 (1.3, 159.8)**	**44.0 (2.2, 896.1)**
Transposition of the great arteries	-	-	0.4 (0.2, 1.1)	0.4 (0.2, 1.1)	-	-
Tetralogy of Fallot	1.9 (0.3, 14.0)	1.6 (0.2, 11.6)	1.3 (0.6, 2.9)	1.1 (0.4, 3.0)	-	-
Ventricular septal defect	0.9 (0.5, 1.7)	0.9 (0.5, 1.7)	0.9 (0.7, 1.1)	0.9 (0.7, 1.1)	0.7 (0.4, 1.3)	0.7 (0.4, 1.4)
Atrial septal defect	0.7 (0.3, 1.9)	0.7 (0.2, 1.8)	0.9 (0.7, 1.2)	0.8 (0.6, 1.1)	1.4 (0.8, 2.5)	1.0 (0.5, 1.8)
Atrioventricular septal defect	0.9 (0.1, 6.5)	0.8 (0.1, 5.9)	0.6 (0.3, 1.2)	0.3 (0.1, 0.8)	1.3 (0.3, 5.3)	0.7 (0.1, 3.6)
Pulmonary valve atresia and stenosis	1.9 (0.7, 5.2)	1.8 (0.7, 4.9)	0.9 (0.6, 1.4)	0.8 (0.5, 1.4)	2.0 (0.9, 4.7)	1.7 (0.7, 4.3)
Tricuspid valve atresia and stenosis	-	-	1.3 (0.3, 5.2)	1.5 (0.3, 7.0)	-	-
Ebstein anomaly	-	-	1.4 (0.4, 4.5)	0.6 (0.1, 2.2)	-	-
Aortic valve stenosis	-	-	1.3 (0.6, 3.0)	1.0 (0.4, 2.9)	-	-
Hypoplastic left heart syndrome	2.1 (0.3, 15.6)	2.2 (0.3, 17.9)	0.5 (0.1, 1.7)	0.5 (0.1, 2.0)	1.5 (0.2, 11.2)	1.2 (0.2, 7.7)
Patent ductus arteriosus	**3.4 (2.0, 5.8)**	**3.2 (1.8, 5.4)**	0.8 (0.6, 1.1)	0.6 (0.4, 1.0)	0.7 (0.3, 1.9)	0.5 (0.2, 1.5)

	NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)	
	PR[b] (95% CI)	PR[bc] (95% CI)	PR[b] (95% CI)	PR[bc] (95% CI)	PR[b] (95% CI)	PR[bc] (95% CI)
Coarctation of the aorta	0.8 (0.1, 5.9)	0.9 (0.1, 6.5)	0.7 (0.4, 1.4)	0.5 (0.2, 1.1)	0.6 (0.1, 4.2)	0.5 (0.1, 3.5)
Cardiovascular						
Total anomalous pulmonary venous connection	**9.9 (1.1, 89.5)**	8.1 (0.9, 74.8)	0.8 (0.1, 7.0)	0.3 (0.0, 5.0)	**14.1 (2.5, 78.5)**	6.4 (0.7, 61.8)
Interrupted aortic arch	-	-	-	-	-	-
Double outlet right ventricle	**6.6 (1.5, 29.6)**	**5.2** (1.0, 28.3)	1.3 (0.5, 3.7)	1.8 (0.5, 6.1)	**4.7 (1.1, 21.2)**	2.6 (0.4, 15.7)
Subtotal	*1.4 (1.0, 2.0)*	*1.3 (0.9, 1.9)*	*0.8 (0.7, 1.0)*	*0.8 (0.6, 0.9)*	*1.0 (0.7, 1.4)*	*0.8 (0.6, 1.2)*
Orofacial						
Cleft palate alone	-	-	1.2 (0.6, 2.1)	1.2 (0.6, 2.4)	1.4 (0.3, 5.8)	1.0 (0.2, 4.7)
Cleft lip alone	-	-	0.4 (0.1, 1.2)	0.4 (0.1, 1.3)	-	-
Cleft lip with cleft palate	-	-	1.3 (0.7, 2.4)	0.9 (0.5, 1.8)	-	-
Subtotal	-	-	*1.0 (0.6, 1.5)*	*0.9 (0.6, 1.4)*	*0.6 (0.2, 2.4)*	*0.4 (0.1, 1.8)*
Gastrointestinal						
Esophageal atresia/ tracheoesophageal fistula	-	-	0.4 (0.1, 1.2)	0.4 (0.1, 2.1)	-	-
Rectal and large intestinal atresia/ stenosis	**5.3 (1.9, 15.0)**	**5.9 (2.1, 17.0)**	0.8 (0.4, 1.8)	0.9 (0.3, 2.2)	0.9 (0.1, 7.9)	1.2 (0.1, 9.7)
Pyloric stenosis	0.3 (0.1, 2.4)	0.3 (0.0, 2.0)	1.2 (0.9, 1.7)	0.9 (0.6, 1.3)	-	-
Hirshsprung's disease	-	-	0.2 (0.0, 1.3)	0.2 (0.0, 2.8)	1.6 (0.2, 11.8)	1.7 (0.2, 18.9)
Small intestinal atresia/stenosis	-	-	0.6 (0.2, 1.6)	0.4 (0.1, 1.8)	1.3 (0.2, 9.5)	0.8 (0.1, 6.3)
Subtotal	*0.9 (0.4, 2.3)*	*0.8 (0.3, 2.1)*	*0.9 (0.7, 1.2)*	*0.8 (0.5, 1.1)*	*0.4 (0.1, 1.3)*	*0.3 (0.1, 1.0)*
Genitourinary						
Renal agenesis/hypoplasia	1.9 (0.3, 14.0)	2.4 (0.3, 18.5)	1.2 (0.5, 2.7)	1.0 (0.4, 2.8)	-	-
Obstructive genitourinary defect	1.6 (0.7, 4.0)	1.7 (0.7, 4.1)	0.7 (0.5, 1.1)	0.6 (0.4, 1.0)	0.9 (0.3, 2.5)	0.7 (0.3, 2.0)
Hypospadias	1.2 (0.6, 2.3)	1.2 (0.6, 2.3)	0.3 (0.2, 0.4)	0.3 (0.2, 0.4)	0.5 (0.2, 1.1)	0.5 (0.2, 1.3)
Subtotal	*1.2 (0.7, 2.1)*	*1.2 (0.7, 2.1)*	*0.4 (0.3, 0.6)*	*0.4 (0.3, 0.5)*	*0.6 (0.3, 1.2)*	*0.6 (0.3, 1.1)*
Musculoskeletal						
Limb deficiencies	1.4 (0.2, 10.0)	1.2 (0.2, 9.2)	1.4 (0.7, 2.7)	0.8 (0.4, 1.7)	2.0 (0.5, 8.2)	1.3 (0.3, 6.1)
Gastroschisis	-	-	0.5 (0.2, 1.1)	0.4 (0.2, 1.1)	-	-
Omphalocele	-	-	1.3 (0.5, 3.5)	0.9 (0.3, 2.7)	-	-
Congenital hip dislocation	-	-	1.2 (0.4, 3.4)	1.6 (0.5, 5.2)	2.2 (0.3, 16.7)	3.0 (0.6, 15.9)
Musculoskeletal						

	NH[a] Black (n=1,680)		Hispanic (n=21,654)		Marshallese (n=2,488)	
	PR[b] (95% CI)	**PR[bc] (95% CI)**	**PR[b] (95% CI)**	**PR[bc] (95% CI)**	**PR[b] (95% CI)**	**PR[bc] (95% CI)**
Diaphragmatic hernia	4.6 (1.4, 15.1)	4.3 (1.2, 15.3)	0.4 (0.1, 1.2)	0.3 (0.1, 1.2)	-	-
Craniosynostosis	0.7 (0.1, 5.5)	0.9 (0.1, 6.4)	0.8 (0.5, 1.5)	1.0 (0.5, 2.0)	-	-
Clubfoot	0.8 (0.2, 3.3)	0.8 (0.2, 3.3)	0.8 (0.5, 1.3)	0.7 (0.4, 1.2)	0.6 (0.2, 2.4)	0.5 (0.1, 2.0)
Subtotal	*0.9 (0.4, 2.0)*	*0.9 (0.38, 1.9)*	*0.8 (0.6, 1.1)*	*0.7 (0.5, 1.0)*	*0.4 (0.2, 1.2)*	*0.4 (0.1, 0.9)*
Chromosomal						
Trisomy 21	0.5 (0.1, 3.6)	0.5 (0.1, 3.5)	1.7 (1.2, 2.5)	1.3 (0.8, 2.1)	1.1 (0.3, 3.4)	0.9 (0.3, 3.2)
Total births with defects	0.9 (0.7, 1.3)	0.9 (0.7, 1.3)	0.8 (0.7, 0.8)	0.7 (0.6, 0.8)	0.8 (0.6, 1.1)	0.7 (0.5, 0.9)

[a] NH=Non-Hispanic

[b] PR=Prevalence Ratio

[c] Adjusted for maternal age, education, parity, and marital status