

RISK FOR FATHERING CHILDREN WITH BIRTH DEFECTS AMONG ARMY CHEMICAL CORPS VIETNAM VETERANS WHO SPRAYED DEFOLIANT IN VIETNAM

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Abstract

There has been concern that offspring of Vietnam veterans, particularly those who were exposed to Agent Orange (defoliant), were at an increased risk for birth defects. This study compares parental-reported birth defect information for index pregnancies of 963 Vietnam and 1055 non-Vietnam veterans who were also classified as to Agent Orange exposure. Birth defect descriptions were reviewed by two pediatricians to determine likelihood and severity. Multiple logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI) adjusting for various factors. Vietnam veterans were significantly more likely (OR=1.55; 95% CI: 1.13, 2.13) to report birth defects than non-Vietnam veterans. However, there was no statistically significant association between pediatrician coded likely and severe birth defects and Vietnam service (OR=0.93; 95% CI: 0.44, 1.98 and OR=0.62; 95% CI: 0.26, 1.48). Sprayers of Agent Orange were significantly more likely to report birth defects (OR=1.48; 95% CI: 1.05, 2.05) and severe birth defects (OR=3.29; 95% CI: 1.91-5.66) than non-sprayers, but there were no significant differences between sprayers and non-sprayers when examining pediatrician coded likely and severe birth defects (OR=0.67; 95% CI: 0.32, 1.41 and OR=0.45; 95% CI: 0.17, 1.18). Although Vietnam veterans and sprayers are more likely to report birth defects, the birth defects as coded by pediatricians do not support an association between Vietnam service and defoliant spraying and birth defects.

Introduction

There have been several studies that have investigated the reproductive outcomes of Vietnam veterans¹⁻⁷. The studies of reproductive outcomes among males have mostly shown that service in Vietnam was not associated with birth defects, spontaneous abortion, stillbirth, or neonatal death²⁻⁶. A study among female veterans found that the risk of moderate-to-severe birth defects was significantly elevated among Vietnam veterans¹. Based on evidence from two studies, an Institute of Medicine panel proposed an association between herbicide exposure in Vietnam and an increased risk of spina bifida in children⁶⁻⁸. United States Army Chemical Corps veterans handled and sprayed herbicides in Vietnam resulting in exposure to Agent Orange and its contaminant, dioxin. The objective of this study was to determine if there was an association between Vietnam service and birth defects as well as if there was an association between military occupational exposure to Agent Orange and birth defects.

Materials and Methods

A health survey of 1499 Vietnam veterans and a comparison group of 1428 non-Vietnam veterans assigned to chemical operations jobs was conducted using a computer-assisted telephone interview (CATI) system during 1999-2000. The Vietnam veteran group was selected to include men whose permanent tour of duty included service in Vietnam reflecting any chemical operations duties between July 4, 1965 and March 28, 1973. The non-Vietnam veteran comparison group was composed of men who had similar characteristics as the study group with respect to branch of service, time period of service, and military occupation with the exception that their permanent tours of duty did not include service in Vietnam. A portion of the health interview survey collected self-reported data on the outcome of each pregnancy fathered by the respondent. The survey also collected information about the mother during each listed pregnancy.

One pregnancy per each respondent was identified as the index pregnancy. For the Vietnam veterans, it was defined as the first pregnancy after at least one year from their entrance date to Vietnam service. For non-

Vietnam veterans, it was defined as the first pregnancy following one year after either July 4, 1965, the starting date for the US ground troops involvement in Vietnam, or the entrance date into military service whichever was later. It is assumed that if there was an effect from Vietnam service that it would be more likely to be manifest in the first pregnancy following at least one year of exposure (defined as Vietnam service and/or handling or spraying of Agent Orange).

A birth defect was defined as a live birth with an affirmative answer from the veteran to one of the following questions: 'Was this child born with any type of birth defect or malformation that was diagnosed by a doctor either at birth or later on?' or 'Did the doctor ever say that this child had an unusual shaped head, wide set eyes, or low set ears?'. Birth defects identified at birth were limited to those defects that were identified before the child left the hospital. Severe birth defects were defined as those defects in which the father answered that the defect required medical treatment, surgery, or limited activities of the child. Since the index pregnancies in this study had occurred 30 or more years ago, it was not feasible to obtain medical records to document the self-report of severity or types of birth defects. All defects for which a description was provided were reviewed independently by two pediatricians who were blinded as to the exposure status. The reported birth defects were grouped into one of eleven groups as follows: likely congenital birth defects including chromosomal abnormality, multiple anomalies of two or more defects in different organ systems, isolated anomalies of one or more defect within the same organ system, congenital neoplasms, heritable genetic diseases/syndromes, unspecified heart abnormalities, and poorly specified non-cardiac defects; and unlikely congenital birth defect including developmental disorders, perinatal complications, miscellaneous pediatric illnesses, and not classifiable. The pediatricians also reviewed the descriptions and rated the likely defects as severe, not severe, or not classifiable based on the verbatim text. If more than one birth defect was reported for an index pregnancy, coding was based on the most severe defect. A pediatrician defined likely birth defect had to have been coded as likely by both pediatricians. A pediatrician defined severe likely birth defect had to have been coded as severe by both pediatricians. For those birth defects where there was disagreement between the pediatricians, the defect was coded as uncertain as to likelihood or severity.

Because prior analysis had shown that self-reported history of spraying Agent Orange was supported by serum TCDD levels, a veteran's self-reported history of spraying Agent Orange was used for the purpose of classifying the veterans into exposure categories⁹.

In order to describe the association between exposure and the risk of each outcome, the odds ratio (OR) and 95% confidence interval (95% CI) were calculated using multivariate logistic regression models to adjust for covariates. Final logistic models included Vietnam service (Vietnam vs. non-Vietnam), a history of spraying herbicide while in the military (sprayer vs. non-sprayer), maternal prenatal care (yes vs. no), maternal smoking during pregnancy (yes vs. no), maternal drinking during pregnancy (yes vs. no), maternal age at birth (as a continuous variable in years), veteran's race (white vs. non-white), and veteran's age at birth (as a continuous variable in years). A subgroup analysis was also performed among only the Vietnam veterans to assess if the association between exposure (spraying Agent Orange) and outcome in this group differed from the overall result using both Vietnam and non-Vietnam veterans. All analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

Results and Discussion

There were a total of 2018 index pregnancies (963 Vietnam and 1055 non-Vietnam). While all of these were singleton pregnancies, 37 of these had two reported birth defects. From the index pregnancies, there were 1740 live births (828 Vietnam and 912 non-Vietnam). A comparison of demographic and pregnancy characteristics revealed that in general the groups were similar, but non-Vietnam sprayers were more likely to be non-white and were slightly younger at the time of the index pregnancy. Vietnam non-sprayers and non-Vietnam sprayers were also less educated while non-Vietnam non-sprayers were less likely to have ever been smokers. Approximately 80% of the index pregnancies had reported prenatal care; 23-31% were not first pregnancies; almost 12% reported maternal drinking during pregnancy; close to 20% reported maternal smoking during pregnancy; the average age of the father at birth was 26 years; and the average age of the mother at birth was 25

years. A majority of the respondents were white (63-82%) and had less than a four year college education (59-78%).

The outcomes of the index pregnancies are presented in Table 1 comparing Vietnam to non-Vietnam, sprayer to non-sprayer, and the subgroup analysis of Vietnam sprayer to Vietnam non-sprayer. After adjustment for demographic characteristics, factors associated with pregnancy, and spraying status, Vietnam veterans were 1.55 times more likely (95% CI: 1.13, 2.13) to report birth defects than non-Vietnam veterans. However, when these were coded by a pediatrician for severity and likelihood, there were no significant differences between Vietnam and non-Vietnam veterans for likely birth defects among their children (OR=0.93; 95% CI: 0.44, 1.98). Sprayers were significantly more likely to report birth defects (OR=1.48, 95% CI: 1.05, 2.05), birth defects identified at birth (OR=2.53, 95% CI: 1.57, 4.07), and severe birth defects than non-sprayers (OR=3.29; 95% CI: 1.91, 5.66). However, using the pediatrician coded likelihood and severity categories resulted in no significant differences between sprayers and non-sprayers for likely birth defects among their children (OR=0.67; 95% CI: 0.32, 1.41). Among the Vietnam veteran subgroup, the results were similar with sprayers significantly more likely to report birth defects identified at birth and severe birth defects than non-sprayers, but using the pediatrician coded likelihood and severity categories resulted in no significant differences between sprayers and non-sprayers in the Vietnam subgroup. There were only three reported cases of spina bifida, two of which were reported by non-Vietnam non-sprayers and one by a Vietnam sprayer. Although Vietnam veterans and sprayers are more likely to report birth defects, an analysis of the birth defects as coded by pediatricians does not support an association between Vietnam service and birth defects or defoliant spraying and birth defects.

The main limitation of this study was the reliance on self-reported birth defects and the inability to confirm what was reported by the veterans based on medical record reviews. A second limitation is that the survey was asking for fathers to report the birth defect information and maternal characteristics during pregnancy. Due to the length of time between the birth and survey, recall of these factors may have been incorrect. A major strength of this study was in the selection of a veteran control group that was similar to the study group except for service in Vietnam. In addition, the exposure status for many of the Vietnam veterans was well characterized using a combination of military occupational history and serum TCDD concentrations. These results are in part consistent with results from other studies looking at paternal reported reproductive outcomes.²⁻⁶

References

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Table 1. Comparison of Birth Defects

Outcomes	Vietnam (828) N (%)	Non-Vietnam (912) N (%)	Adjusted Odds Ratio (95% CI)
Veteran reported birth defects	153 (19)	113 (12)	1.55 (1.13, 2.13)
Veteran reported birth defects identified at birth	66 (8)	43 (5)	1.21 (0.75, 1.96)
Veteran reported severe birth defects ^a	50 (6)	34 (3)	0.99 (0.57, 1.71)
Pediatrician defined likely birth defects	66 (8)	53 (6)	0.93 (0.44, 1.98)
Pediatrician defined severe likely birth defects	17 (2)	22 (2)	0.62 (0.26, 1.48)
	Sprayer (466) N (%)	Non-Sprayer (1232) N (%)	Adjusted Odds Ratio (95% CI)
Veteran reported birth defects	96 (21)	166 (14)	1.48 (1.05, 2.05)
Veteran reported birth defects identified at birth	51 (11)	56 (5)	2.53 (1.57, 4.07)
Veteran reported severe birth defects ^a	44 (9)	38 (3)	3.29 (1.91, 5.66)
Pediatrician defined likely birth defects	41 (9)	76 (6)	0.67 (0.32, 1.41)
Pediatrician defined severe likely birth defects	8 (2)	31 (3)	0.45 (0.17, 1.18)
	Vietnam Sprayer (374) N (%)	Vietnam Non-Sprayer (439) N (%)	Adjusted Odds Ratio (95% CI)
Veteran reported birth defects	78 (21)	74 (17)	1.34 (0.91, 1.97)
Veteran reported birth defects identified at birth	41 (11)	24 (6)	2.26 (1.26, 4.04)
Veteran reported severe birth defects ^a	35 (9)	14 (3)	3.03 (1.51, 6.11)
Pediatrician defined likely birth defects	33 (9)	32 (7)	0.70 (0.28, 1.72)
Pediatrician defined severe likely birth defects ^a	6 (2)	11 (3)	0.47 (0.14, 1.53)

^a "Severe birth defects" determined by the veteran reporting that the defect required treatment, surgery, or that the defect limited the activity of the child.