Rates of Congenital Anomalies and Other Adverse Birth Outcomes in an Offspring Cohort of Registered Nurses from British Columbia, Canada

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ABSTRACT

Objectives: Although there is concern that occupational exposures in some nursing professions may confer reproductive risks, there are few relevant studies. Our objective is to determine if a cohort of female registered nurses (RN) from British Columbia (BC), in comparison to BC women in general, have elevated rates of congenital anomalies, stillbirths, low birth weight, or prematurity in their offspring.

Methods: A cohort of RNs from BC was linked to Vital Statistics birth records and the BC Health Status Registry (HSR) between the years 1986 and 2000. The RN offspring cohort included 23,222 births. For each outcome, odds ratios (OR) with 95% confidence intervals (CI) were determined by comparing rates in the nurses' cohort with the rates in the general population standardized for the year of birth.

Results: Apart from chromosomal anomalies, for each of the ICD-9 congenital anomaly categories there were fewer congenital anomalies than expected, resulting in an overall prevalence of congenital anomaly cases (with at least one anomaly) that was significantly lower in the RN cohort (1,567 observed vs. 1,846 expected; OR 0.84, 95% CI 0.78-0.90) in comparison to the general population. Low birth weight (1,138 observed vs. 1,260 expected; OR 0.90, 95% CI 0.83-0.98) was also significantly lower, while prevalence of prematurity and stillbirths were not significantly different than among the general population.

Conclusion: Offspring of RNs in BC had a lower prevalence of congenital anomalies and low birth weight compared to the rates found among the general population. Further studies are underway to determine if subpopulations within the RN cohort are at risk.

Key words: Congenital abnormalities; pregnancy outcomes; birth weight; nurses

La traduction du résumé se trouve à la fin de l'article.

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A variety of chemicals inherent to occupational environments have the potential to influence prenatal development, resulting in such adverse birth outcomes as congenital anomalies, stillbirths, low birth weight, and prematurity.¹⁻⁴ A congenital anomaly is any structural (most common), functional, or biochemical abnormality that is present at birth.⁵ Approximately 15-25% of congenital anomalies are due to known genetic conditions (e.g., chromosomal anomalies) and the remaining cases are suspected to have some degree of environmental influence.⁵

Health care workers are exposed to a variety of workplace hazards that can result in adverse reproductive outcomes.⁶ There are more than 2.5 million registered nurses employed in the US⁷ and 250,000 in Canada,⁸ who are potentially exposed to suspected reproductive hazards including anaesthetic gases, antineoplastic drugs, ionizing radiation, sterilizing agents, disinfectants, and infectious agents.^{9,10}

There are numerous case reports describing individual occupational health hazards in the nursing professions, but epidemiological evidence of reproductive risks related to occupational hazards for nurses is relatively scarce. A registry-based cohort study of nurses in Norway during 1970-1973 showed that first-born children of mothers who were nurses had an elevated relative risk of malformations compared to non-working mothers.¹¹ A data linkage study completed in Atlanta, Georgia comparing cases of birth defects with geographic and race matched healthy controls showed that offspring of mothers employed within the nursing field had a modest increased risk of birth defects.¹² Conversely, two studies noted a

lower proportion of birth defects in offspring of nurses compared to reference populations.^{13,14}

The aims of our study were to determine: a) if a cohort of female RNs in the province of British Columbia (BC), in comparison to the general BC population, had an elevated prevalence of congenital anomalies, stillbirths, low birth weight and prematurity in their offspring and b) whether certain maternal and infant characteristics were associated with these outcomes.

METHODS

The design of the study involved linking administrative data to a retrospective cohort of RNs in BC. In 2003, we obtained data on 56,176 RNs who were registered for at least one year with their

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Table 1. Prevalence and Odds Ratios of RN Offspring Cohort Variables and Birth Outcomes Compared to Those of the BC Population, Adjusted for Year of Birth

	Observed		Expected*	OR	CI (95%)	p-value†
	n	%				
Birth Outcomes						
Stillbirths						
No	23,075	99.4%	23,062	1.00		0.458
Yes	147	0.6%	160	0.92	0.73-1.15	
Multiplicity‡						
Single	22,491	97.4%	22,579	1.00		0.022
Twin	560	2.5%	479	1.17	1.04-1.33	
Triplet	24	0.1%	17	1.41	0.76-2.64	
Gestational Age§ (weeks)						
Premature (<37)	1555	6.7%	1551	1.00	0.93-1.07	0.193
Normal (37-41)	20,709	89.2%	20,634	1.00		
Post mature (>41)	950	4.1%	1029	0.92	0.84-1.01	
Birth Weight§						
Low (<2500g)	1138	4.9%	1260	0.90	0.83-0.98	0.002
Normal (2500-4499g)	21,483	92.4%	21,440	1.00		
High (≥4500g)	592	2.6%	512	1.15	1.02-1.30	
Congenital Anomalies						
None	21,655	93.3%	21,376	1.00		
Cases (any diagnoses)	1567	6.7%	1846	0.84	0.78-0.90	<0.001
Descriptive Variables						
Sex§						
Female	11,320	48.8%	11,301	1.00		0.863
Male	11,895	51.2%	11,914	1.00	0.96-1.03	
Mother's Age (years)						
<30	8183	35.2%	13,690	1.00		<0.001
30-34	9673	41.7%	6604	2.45	2.35-2.55	
≥35	5366	23.1%	2928	3.07	2.91-3.23	
Total cohort	23,222	100.0%	23,222			

* Expected frequencies based on BC rates and adjusted for year of birth.

† Significance of the trend, based on chi-square analysis of observed and expected frequencies.

‡ Prevalence of congenital anomalies among multiple births for BC population unavailable for total births; figures based on single births among RN cohort and BC population.

§ Unknown values for sex (n=7), gestational age (n=8) and birth weight (n=9) excluded; figures based on reduced frequencies.

provincial regulatory body between 1974 and 2000, inclusive.¹⁵ Work histories, based on yearly registration renewals completed by the nurses, contained data about the date of initial registration, educational level, and employment-specific information on place, position, and field of employment for each year the subjects were registered as practicing RNs.

The offspring cohort was established by linking the RN cohort database to live and stillbirth records from the BC Vital Statistics Agency marriage and birth files (approximately 670,000 files). Identifiers available in the RN database for linkage included mother's names, birth date, location of maternal residence (city, postal codes, local health area). Relevant vital statistics records included child's birth date, sex, gestational age, birth weight, multiplicity (twins, triplets), and live or stillbirth status. Rules for scoring agreement and disagreements on surname, given names and day, month and year of birth were based upon the generalized iterative record linkage system.¹⁶

Birth registration records were linked to the BC Health Status Registry (HSR) in order to obtain information on the presence and type of congenital anomalies. The HSR was established in 1952 to ascertain, record and classify "handicapping" conditions and congenital anomalies in BC. The HSR receives health information about children up to the age of 20 years from over 80 registering sources, including government agencies concerned with health and human resources, hospitals, treatment and rehabilitation centres, voluntary agencies, physicians, and the vital registration system. Because recording practices were less consistent in earlier periods of surveillance, BC Vital Statistics limited data from the HSR to the 1986 to 2000 time period to ensure consistency in data quality.

The disease conditions obtained from the HSR were coded according to the 9th edition of the World Health Organization's

International Classification of Disease (ICD-9: codes 740 to 759) with the year 2000 cases recoded according to the ICD-10 classification. The four-digit ICD-9 codes were categorized into congenital anomaly groupings used by BC Vital Statistics, as shown in Table 3. Elective termination data were unavailable for the years studied.

The study was approved by the University of British Columbia's Clinical Research Ethics Board. All files were stripped of identifying information. Following data accuracy verification and re-linkage of the files, the final offspring cohort totalled 23,222 births, among 12,855 RN mothers. Multiple adverse reproductive outcomes were treated as independent outcomes. All continuous variables were categorized: gestational age (premature <37 weeks, mature/normal 37-41 weeks, and post-mature >41 weeks); birth weight (low birth weight <2500g, normal birth weight 2500-4499g, and high birth weight ≥4500g); year of birth (1986-1990, 1991-1995, and 1996-2000); mother's age at birth (<30 years, 30-34 years, ≥35 years); and RN mother's educational attainment (diploma, undergraduate degree, and graduate degree). Missing values resulted in the case being excluded from analyses involving that variable.

The rates of each birth outcome for each variable, calculated for each year of birth category (see above) from Vital Statistics and published BC general population data,^{17,18} were then applied to the respective birth count for that year category from the RN offspring cohort and summed to derive an expected count adjusted by year of birth. To compare the rates of reproductive outcomes and maternal characteristics between the RN offspring cohort and the BC population, odds ratios (OR) with 95% confidence intervals (CI) were calculated, representative of relative risk. The chi-square statistic was used to compare cross-tabulations of the observed and expected counts among the RN offspring cohort for each predictor. Further cross-tabulations with OR and CI were calculated for

Table 2. Prevalence and Odds Ratios for Potential Risk Factors of Congenital Anomalies within the RN Offspring Cohort (n=23,222)*

	No Congenital Anomalies†	Cases	% Cases	OR	CI (95%)	p-value‡
Stillbirths						
No	21,538	1537	6.7%	1.00		<0.001
Yes	117	30	20.4%	3.59	2.40-5.38	
Multiplicity						
Single	21,105	1508	6.7%	1.00		0.013
Twin	525	56	9.6%	1.49	1.13-1.98	
Triplet	25	3	10.7%	1.68	0.51-5.57	
Gestational Age§ (weeks)						
<37	1347	208	13.4%	2.32	1.98-2.71	<0.001
37-41	19,416	1293	6.2%	1.00		
>41	884	66	6.9%	1.12	0.87-1.45	
Birth weight§						
Low (<2500g)	951	187	16.4%	2.96	2.51-3.49	<0.001
Normal (2500-4499g)	20,144	1339	6.2%	1.00		
High (≥4500g)	552	40	6.8%	1.09	0.79-1.51	
Sex§						
Female	10,630	690	6.1%	1.00		<0.001
Male	11,018	877	7.4%	1.23	1.11-1.36	
Mother's Age (years)						
<30	7653	530	6.5%	1.00		0.142
30-34	9029	644	6.7%	1.03	0.91-1.16	
≥35	4973	393	7.3%	1.14	0.99-1.31	
Mother's Education						
Diploma	16,065	1188	6.9%	1.00		0.363
Undergraduate degree	5237	355	6.3%	0.92	0.81-1.04	
Graduate degree	353	24	6.4%	0.92	0.61-1.40	
Total cohort	21,655	1567	6.7%			

* Case defined as having one or more diagnosis of a congenital anomaly as categorized in ICD-9.

† Births with no congenital anomalies.

‡ Significance of the trend, based on chi-square analysis.

§ Unknown values for sex (n=7), gestational age (n=8) and birth weight (n=9) excluded; figures based on reduced frequencies.

the distribution of each predictor by congenital anomalies among the RN offspring cohort. Observed and expected frequencies were then calculated for each category of congenital anomalies. To compare the rates between the RN cohort and the BC population, standard incidence ratios (SIR) of observed over expected frequencies, with 95% confidence intervals, were calculated. For all analyses, a two-sided significance level of $p < 0.05$ was used.

RESULTS

Table 1 shows the distribution of reproductive outcomes, and variables, among the RN offspring cohort, as well as expected frequencies for each variable derived from rates among the BC general population. The prevalence of low birth weight and congenital anomalies were significantly lower in the RN offspring cohort, while high birth weight and multiplicity (twins) were significantly higher. The average number of diagnoses per case for the RN cohort was 1.44 compared with 1.51 among the BC general population.

Within the RN cohort (Table 2), births that were premature or low in birth weight, stillbirths, as well as twins and triplets, had a higher prevalence of congenital anomalies. There were more cases of congenital anomalies in males (7.4% vs. 6.1%; OR 1.23, 95% CI 1.11-1.36), accounted for by an increased prevalence of genital anomalies. The sex ratios were the same (1.05) for the RN cohort and the BC population. A greater proportion of RNs gave birth in the older age group compared to the BC population. The majority of RNs had a diploma (74%), 24% had an undergraduate degree and 1.6% had a graduate degree, but there was no statistical difference in congenital anomalies between the groups.

Table 3 shows the distribution of categorized congenital anomalies cases with comparisons to expected frequencies based on the BC general population. The number of total cases (with at least one congenital anomaly) and number of specific congenital anomalies (diagnoses) were lower than expected. Apart from chromosomal anomalies, for each of the ICD-9 categories, there were fewer con-

genital anomalies than expected. The most notable reductions were seen in heart defects (SIR 0.52; 95% CI 0.45-0.61), cleft lip and palate (SIR 0.47; 95% CI 0.34-0.65) and the number of cases with multiple anomalies (SIR 0.43; 95% CI 0.26-0.67).

DISCUSSION

Record linkage between the RN offspring cohort with the BC Vital Statistics birth registry effectively enabled the assessment of suspected reproductive health risks inherent to the nursing profession. Offspring from this cohort had a lower prevalence of congenital anomalies and low birth weight than those of the BC population. Stillbirths and prematurity were comparable to the BC general population, while the prevalence of twins and high birth weight were higher. Within the RN offspring cohort, stillbirths, male infants, those with low birth weight, prematurity and twins were significantly more likely to have at least one birth defect.

The prevalence of congenital anomalies was 6.7% among the offspring RN cohort which is higher than the prevalence observed in other large-scale studies, ranging from 3.8%¹¹ to 5.2%.¹⁴ Our higher incidence may be accounted for by a longer period of ascertainment (until 20 years of age for the HSR) and perhaps inclusion of more minor diagnoses (e.g., some integumentary anomalies) compared to most studies. For the same time period in the general BC population, the prevalence of birth defects was 7.9%, which is also higher than estimates seen in other general populations. For example, the prevalence of birth defects was 5.8% and 4.8% respectively for the years 1986-2000 in the Alberta Congenital Anomalies Surveillance System,¹⁹ and the Canadian Congenital Anomalies Surveillance System (Personal Communication: Jocelyn Rouleau, Canadian Congenital Anomalies Surveillance System, Public Health Agency of Canada, April 6, 2009), both data bases using information, at that time, collected on births until one year of age.

Consistent with our study, two previous studies noted a lower proportion of birth defects in offspring of nurses compared to those

Table 3. Distribution and Standard Incidence Ratios (SIR) of Congenital Anomalies by Category* among Offspring of the RN Cohort (n=23,222)

Congenital Anomaly Category†	ICD-9 Code	Observed		Expected‡	SIR‡	CI (95%)
		n	%	n		
Nervous System	740-742	69	3.6%	119	0.58	0.45-0.74
Eye	743	99	5.2%	119	0.83	0.67-1.01
Ear, Face, Neck	744	99	5.2%	163	0.61	0.49-0.74
Heart	745-746	164	8.5%	313	0.52	0.45-0.61
Circulatory System	747	155	8.1%	227	0.68	0.58-0.80
Respiratory System	748	65	3.4%	79	0.82	0.63-1.05
Cleft Palate/Lip	749	38	2.0%	80	0.47	0.34-0.65
Upper Alimentary Tract	750	92	4.8%	146	0.63	0.51-0.77
Other Digestive System	751	46	2.4%	71	0.65	0.48-0.87
Genital	752	239	12.4%	327	0.73	0.64-0.83
Urinary System	753	112	5.8%	146	0.76	0.63-0.92
Musculoskeletal System	754-756	510	26.5%	676	0.75	0.69-0.82
Integumentary System	228, 757	109	5.7%	141	0.77	0.63-0.93
Chromosomal Anomalies	758	79	4.1%	79	1.01	0.80-1.25
Multiple Anomalies	759.7-759.8	19	1.0%	45	0.43	0.26-0.67
Other/Unspecified Anomalies§	759.0-759.6, 759.9, 237.7	27	1.4%	42	0.64	0.42-0.93
Total Diagnoses	740-759.9	2258		2773	0.81	0.78-0.85
Total Cases	740-759.9	1567		1842	0.85	0.81-0.89

* Cases are represented more than once across categories if there are multiple anomalies present, but multiple diagnoses within a category of the same case is only counted once in that category. Therefore, neither total diagnoses nor total cases are summations of the cases for each category.

† Categories as defined by BC Vital Statistics.

‡ SIR derived from observed/expected (based on BC rates and adjusted for year of birth).

§ Includes anomalies of the spleen, adrenal gland, and other endocrine glands; situs inversus; conjoined twins; tuberous sclerosis; other hamartoses; and unspecified diagnoses.

of reference populations. The first was a study on almost 3,000,000 births during 1980,¹⁴ and the second was a small study of nurses employed in operating rooms from 1973 to 1975.¹³ In contrast, a case-control study of 4,915 cases and 3,027 randomly selected healthy controls (frequency matched for geographic region, hospital of birth, race, year of birth and quarter of year) between 1968 and 1980 found that the offspring of mothers employed in a nursing occupation while pregnant had a relative risk of 1.42 (95% CI 1.06-1.88) for having at least one congenital anomaly.¹²

Many early studies tended to be cross-sectional or anecdotal case studies, self-reported questionnaire-based, and/or of a smaller scale.^{2,20} Such studies are prone to recall biases, poor response rates, limited statistical power to detect significant associations, and non-standardized ascertainment of outcomes. By comparison, our record linkage analysis allowed for more comprehensive ascertainment in that the large sample size enabled sufficient power for assessing outcomes that are generally infrequent. The use of administrative records avoided recall bias, a significant problem for questionnaire-based studies, and having records for the total population of interest avoided selection bias.

Working women in general tend to have more favourable demographic, behavioural, and health-related characteristics than non-working women.¹ Although the BC population data included mothers in other lines of employment, it also included those who were not working. As health care providers, nurses may be more likely to adopt healthier practices when preparing for pregnancy, such as folic acid supplementation, avoidance of alcohol and smoking, and other behaviours protective of fetal health.²¹

A weakness of examining total congenital anomalies is that they are heterogeneous outcomes that include distinct etiologies (e.g., genetic basis) and differential susceptibility to specific teratogenic exposures.^{4,5} Therefore, interpretations of results based on total congenital anomalies are not as meaningful as when the congenital anomalies are grouped into biologically relevant categories.²² The large cohort size afforded this investigative capacity for each category of congenital anomaly. Although most categories were lower,

the rates of heart defects and facial cleft were substantially lower in the RN cohort. Both anomalies may be decreased with folic acid supplementation²³⁻²⁵ and increased with exposures such as alcohol consumption and cigarette smoking,²⁶⁻²⁸ which may reflect the health care providers' level of health promotion knowledge. The significantly higher prevalence of high birth weight infants, however, is concerning and may reflect rates of obesity or gestational diabetes.²⁹

Just as variability exists across categories of congenital anomaly cases, the degree of exposure to suspected teratogens may vary depending on the type of work within the nursing occupation. While this study served as an exploratory tool for investigating the risk of reproductive outcomes among RNs, further internal analyses will allow for investigation of the risk related to different areas of employment within nursing, or levels of exposure to specific teratogens, as estimated from questionnaire and work histories.

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RÉSUMÉ

Objectifs : On craint que les expositions professionnelles dans certains métiers des soins infirmiers présentent des risques génésiques, mais il existe peu d'études sur ce sujet. Nous avons voulu déterminer si la progéniture d'une cohorte d'infirmières autorisées de la Colombie-Britannique (C.-B.), comparativement aux Britanno-Colombiennes en général, présentait des taux élevés d'anomalies congénitales, de mortinatalité, d'insuffisance de poids à la naissance ou de prématurité.

Méthode : Nous avons maillé une cohorte d'infirmières autorisées de la C.-B. avec les dossiers de naissance et le registre de l'état de santé de cette province entre 1986 et 2000. La cohorte d'enfants d'infirmières autorisées comptait 23 222 naissances. Pour chaque résultat, nous avons calculé les rapports de cotes (RC) avec intervalles de confiance (IC) de 95% en comparant les taux dans la cohorte des infirmières aux taux dans la population générale, normalisés pour l'année de naissance.

Résultats : À l'exception des anomalies chromosomiques, il y a eu moins d'anomalies que prévu dans chacune des catégories d'anomalies congénitales de la CIM-9. La prévalence globale des cas d'anomalies congénitales (avec au moins une anomalie) était significativement moins élevée dans la cohorte des infirmières autorisées (1567 cas observés c. 1846 cas attendus; RC = 0,84, IC 95% = 0,78-0,90) que dans la population générale. L'insuffisance de poids à la naissance (1138 cas observés c. 1260 cas attendus; RC = 0,90, IC 95% = 0,83-0,98) était aussi significativement moins élevée, tandis que la prévalence de la prématurité et de la mortinatalité n'était pas significativement différente de celle dans la population générale.

Conclusion : La progéniture des infirmières autorisées en C.-B. a une prévalence plus faible d'anomalies congénitales et d'insuffisance de poids à la naissance que dans la population générale. D'autres études sont en cours pour déterminer si certaines sous-populations de la cohorte des infirmières autorisées sont à risque.

Mots clés : anomalies congénitales; pronostic de la grossesse; poids de naissance; infirmières et infirmiers