Multiple Births Associated With Assisted Human Reproduction in Canada

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Abstract

Objective: Assisted human reproduction has been associated with increased rates of multiple births. Data suggest that twins and higher order multiple pregnancies are at risk for pre- and postnatal health complications that contribute to stress on both the family and the Canadian health care system. No published Canadian data estimate the contribution of assisted human reproduction to multiple birth rates. This study was designed to determine the contributions of age and assisted human reproduction to multiple birth rates in Canada.

Methods: We performed analyses of existing Canadian databases, using a mathematical model from the Centers for Disease Control and Prevention. More specifically, data from the Canadian Vital Statistics: Births and Stillbirths database were combined with data from the Canadian Assisted Reproductive Technologies Register collected by the Canadian Fertility and Andrology Society. Datasets were standardized to age distributions of mothers in 1978.

Results: Results suggest that in vitro fertilization, ovulation induction, and age each contribute more to the rates of triplets than to twins. As expected, the contribution of natural factors was higher to twins than to triplets.

Conclusion: These are the first Canadian data analyzed to separate and measure the contributions of age and assisted reproductive technologies to multiple birth rates. Our findings are important for guiding physician and patient education and informing the development of treatment protocols that will result in lower-risk pregnancies and improved long-term health for women and their offspring.

Key Words: Multiple births, assisted human reproduction, in vitro fertilization, ovarian stimulation, ovulation induction

Competing Interests: None declared.

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Résumé

Objectif : La procréation assistée a été associée à des taux accrus de grossesse multiple. Les données laissent entendre que les grossesses gémellaires et les grossesses multiples de rang élevé sont exposées à des risques de complications de santé prénatales et postnatales qui contribuent au stress qui est imposé à la famille et au système de santé canadien. Aucune donnée canadienne publiée n'a permis d'estimer l'apport de la procréation assistée aux taux de grossesse multiple. Cette étude a été conçue pour déterminer l'apport de l'âge et de la procréation assistée aux taux de grossesse multiple au Canada.

Méthodes : Nous avons mené des analyses portant sur les bases de données canadiennes existantes, au moyen d'un modèle mathématique issu des *Centers for Disease Control and Prevention*. Plus particulièrement, les données issues de la base de données sur les naissances et les mortinaissances du Programme de la statistique de l'état civil du Canada ont été combinées aux données issues du registre canadien des techniques de procréation assistée tenu par la Société canadienne de fertilité et d'andrologie. Les ensembles de données ont été normalisés en fonction de la répartition selon l'âge des mères en 1978.

Résultats : Les résultats semblent indiquer que la fécondation *in vitro*, le déclenchement de l'ovulation et l'âge contribuent tous plus aux taux de grossesse triple qu'aux taux de grossesse gémellaire. Comme prévu, l'apport des facteurs naturels était plus élevé dans le cas des grossesses gémellaires que dans celui des grossesses triples.

Conclusion : Il s'agit des premières données canadiennes à être analysées en vue de distinguer et de mesurer l'apport de l'âge et des techniques de procréation assistée aux taux de grossesse multiple. Nos résultats sont importants pour orienter la sensibilisation des médecins et des patientes, ainsi que pour éclairer l'élaboration de protocoles de traitement qui donneront lieu à des grossesses exposées à des risques moindres et à une amélioration de la santé à long terme des femmes et de leur progéniture.

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INTRODUCTION

Since the mid-1970s, the rate of multiple births in Canada has been steadily rising, from 1.8% of all births throughout the 1970s to 3.0% in 2004.[1] Research into the factors underlying the increase in multiple births has focused on elucidating the contribution of natural factors and the advent of assisted reproductive technologies (the collective name for all procedures used to help people build their families through assisted human reproduction).[2] While the majority of twins are naturally conceived, assisted human reproduction has purportedly resulted in a dramatic increase in the number of multiple births, mainly through the use of ovulation induction and in vitro fertilization. In 2006, more than 30% of pregnancies using assisted reproductive technologies in Canada were twins or higher order multiple gestations (triplets or greater) and more than one half of all neonates born through AHR are the products of multifetal gestations.[3,4] High birth order has been implicated as underlying much of the amplified risk associated with AHR,[5,6] and ovulation induction is thought to be the primary reason underlying the marked increase in higher order multiple pregnancies in the past two decades.[7,8]

Multifetal pregnancies are risky for both the mother and the developing fetuses, with maternal morbidity reported to be seven-fold greater in multiple pregnancies than in singletons.[9] In a Canadian retrospective cohort of 165 188 singleton pregnancies and 44 674 multiple pregnancies from 1984 to 2000, multiple pregnancies were associated with significant increases in cardiac morbidity, hematologic morbidity, amniotic fluid embolus, preeclampsia, gestational diabetes, postpartum hemorrhage, prolonged hospital stay, need for obstetric intervention, hysterectomy, and blood transfusion.[10]

Multifetal gestation also has serious risks for fetal and neonatal outcome. Twins conceived following ART are at higher risk for preterm birth, low birth weight, hospitalization, and death than naturally conceived twins.[11]

ABBREVIATIONS

AHR	assisted human reproduction
ART	assisted reproductive technologies
CARTR	Canadian Assisted Reproductive Technologies Register
CFAS	Canadian Fertility and Andrology Society
HOM	higher order multiple
IVF	in vitro fertilization
OI	ovulation induction without in vitro fertilization

Prematurity is the single greatest cause of morbidity and mortality in perinatology, accounting for 70% of neonatal deaths and up to 75% of neonatal morbidity.[12] Perinatal mortality rates are reported to be four-fold higher in twins (33.1 per 1000) and six-fold higher in triplets (56.2 per 1000) than in singletons (7.4 per 1000), and cerebral palsy rates at one year of age are four-fold higher in children of multiple births (5.9 per 1000) than in singletons (1.4 per 1000).[9,13] In addition to increased risk of cerebral palsy, recent studies highlight the range and severity of cognitive, sensory, linguistic, visual-perceptual, attention, and learning deficits in very preterm children.[14] In cases of long-term neurocognitive deficits, pulmonary dysfunction, and ophthalmologic disorders, families, health care services, and education systems experience the impact of prematurity for the lifetime of the preterm-born child.[3,12]

Parenting multiples has been reported to create increased physical, social, emotional, and financial demands on parents, and these demands are compounded when one or more of the children have a disability resulting from prematurity.[15,16] In addition to the long-term financial burden of raising several children at once, families may find the costs of child care and the extra medical costs associated with prematurity-induced health complications extraordinary. Mothers of multiples are particularly affected, experiencing stress, fatigue, marital strain, social isolation, and a sense of inadequacy at being unable to give each child sufficient attention.[17,18]

Although data strongly suggest that ART makes a significant contribution to multiple births, factors other than assisted reproductive technologies also contribute to the occurrence of multifetal pregnancies. For example, the risk of multifetal pregnancies is higher for women over 32 years of age[19–21] and for those with partners who have high sperm counts or motility.[22,23] The challenge, then, is determining how much of the increase in multiple births in recent years is due to natural factors, such as increased maternal age, and how much might be due to the advent of reproductive technologies.

Determining the contributions of OI and other assisted reproductive technologies to multiple births is important for understanding the risks, implications, and outcomes of AHR on pregnancy and offspring, as well as for decision-making related to policy development, service delivery, patient education, and patient care. To date, no Canadian data exist with respect to the specific contributions of natural factors (e.g., maternal age), OI, and IVF to multiple births. Thus, this study was designed to estimate the contributions of age and assisted human reproduction to multiple births in Canada.