Is Paternal Age Associated with an Increased Risk of Low Birthweight, Preterm Delivery, and Multiple Birth?

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ABSTRACT

Objective: To determine if paternal age elevates the risk of low birthweight (<2500g, LBW), preterm birth (< 37 weeks gestation), and multiple gestation among mothers whose age does not predict an elevated risk.

Design/Methods: Population data on birth outcome, maternal age and paternal age was obtained from Alberta Health and Wellness for all births 1990-1996.

Results: Among women aged 25 to 29, regardless of parity, there was no linear relationship between paternal age and preterm birth or LBW. However, multiple birth rates increased with increased paternal age ($p<0.01$). Among singleton births, advanced paternal age (>50 years) increased the risk of LBW and preterm birth ($p\leq0.05$).

Conclusions: Paternal age is not a risk factor for LBW or preterm delivery among low risk women. The increased risk of multiple birth with increased paternal age, regardless of parity, requires confirmation among other populations.

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

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Acknowledgements: Funding was received from Alberta Health and Wellness and Calgary Health Region. We thank Alberta Health and Wellness for access to the provincial data set.

Low birthweight (LBW, <2500 grams) and preterm delivery (<37 weeks gestation) are recognized causes of infant mortality and morbidity. LBW rates continue to increase and at 6.0%, the LBW rate in Alberta exceeds the Canadian rate of 5.8%.[1] The Alberta rate is comparable to the United States estimate of 7.0%[2] and is higher than rates reported for Finland (4.1%), France (3.8%), Sweden (4.4%) and Switzerland (5.5%).[3,4] Although some international variation in rates may be due to differences in definition (e.g., inclusion/exclusion of stillbirth), Finland, Sweden and Switzerland use definitions similar to Canada, therefore the rates are comparable. To address the issue of LBW, the independent risk factors require further definition.

Much of the research on risk factors has focused on maternal characteristics and it is well documented that maternal age is an independent risk factor for LBW, preterm delivery and multiple birth.[5] Other factors that have been associated with an increased risk of low birthweight or preterm delivery include smoking during pregnancy,[5,6] poor prenatal care,[7,8] poverty,[9] pregnancy complications,[10,11] mental health,[12] genetic factors,[13-17] obstetrical history,[18] and interpregnancy interval.[19,20]

Less well described is the independent impact of paternal age on LBW, preterm delivery and multiple birth. Other research on the influence of paternal factors on birth outcome suggests that, among full-term infants, paternal birthweight influences infant birthweight. Paternal birthweight between 3000-3999 grams reduces infant birthweight by 109 grams compared to a paternal birthweight in excess of 4000 grams. If paternal birthweight is less than 3000 grams, after controlling for covariates, the offspring are anticipated to be 176 grams lighter.[21] Among full-term infants (gestational age ≥ 37 weeks), a paternal height less than 2 standard deviations below the mean reduces infant birthweight by 83 grams compared to a paternal height of 2 standard deviations above the mean.[22] The impact of these variables on the delivery of LBW or preterm infants has not been described.

LBW is the most important determinant of neonatal mortality and morbidity. LBW contributes to approximately 75% of deaths occurring in the first week of life.[18,23,24] Post-discharge, LBW infants can suffer from feeding difficulties, growth

retardation, and issues related to administering medication and care giving.[25,26] Furthermore, these infants often require more medical care throughout the first year of life for respiratory infections, asthma, otitis media, gastro-oesophageal reflux, failure to thrive, colic (irritable baby or distressed baby syndrome) and inguinal hernia.[1,27] LBW infants are at a greater risk of long-term disability and disease including cerebral palsy, visual problems, learning disabilities and respiratory problems.[28,29]

OBJECTIVE

To determine if paternal age elevates the risk of LBW, preterm delivery and multiple birth among mothers whose age does not predict an elevated risk. Second, to determine if maternal and paternal age difference is a factor in these birth outcomes.

DESIGN/METHODS

Population data between 1990 and 1996 on birth outcomes, maternal age and paternal age was obtained from the Alberta Health and Wellness Physician Notice of a Live or Still Birth and Newborn Record. By law, this record is completed for all births occurring in Alberta. Information on birth outcomes such as liveborn, stillborn, gestational age (best estimate as derived from the maternal last menstrual period and antenatal ultrasound examination), multiple birth, gender, birthweight (weight in grams in the delivery room) and visible birth defects are included on the record. All data were double entered, verified, and analyzed using SPSS version 10.0 using bivariate techniques including odds ratios (OR), chi-square tests and comparisons of means. The data were analyzed with regard to the relationship between paternal age and LBW, preterm delivery and multiple birth among singleton births, all births, multiple births and those of first parity. Logistic and linear regression were used to confirm and quantify the risk of outcomes by paternal age, while controlling for maternal age, and to provide an objective measure of the change in risk. Logistic regression allows for the assessment of the independent effect of a variable (paternal age) on the outcome (LBW, preterm and multiple birth) while taking other variables (maternal age) into account.

TABLE I

Maternal Age and Low Birthweight, Preterm Birth and Multiple Birth, Alberta, 1990-1996 (n=283,956)

Maternal Age	< 2500 grams n (%)	< 37 weeks n (%)	Multiple Birth n (%)
≤ 19	1603 (7.3)	1867 (8.4)	261 (1.2)
20-24	3920 (6.5)	4414 (7.3)	1135 (1.9)
25-29	5534 (5.8)	6444 (6.8)	2189 (2.3)
30-34	4735 (6.2)	5528 (7.2)	2016 (2.6)
35-39	1854 (7.2)	2230 (8.7)	709 (2.8)
40-56	239 (7.5)	294 (9.2)	56 (1.8)
Total	17,885 (6.3)	20,777 (7.3)	6366 (2.2)
T-test*	0.006	0.000	0.000
Chi-square trend	0.001	0.001	0.001

* T-test is among women 20 years or greater

TABLE II

The Impact of Paternal Age on Low Birthweight, Preterm Birth and Multiple Birth Among Women Aged 25-29 from Alberta, 1990-1996 (n=90,948)

Paternal Age	< 2500 grams		< 37 weeks		Multiple Birth
	All n (%)	Singleton n (%)*	All n (%)	Singleton n (%)*	n (%)
≤ 19	3 (4.1)	3 (4.1)	4 (5.5)	4 (5.5)	0 (0.0)
20-24	261 (6.6)	221(5.7)	306 (7.7)	268 (6.9)	81 (2.0)
25-29	2287 (5.6)	1840 (4.6)	2686 (6.6)	2258 (5.7)	899 (2.2)
30-34	1937 (5.5)	1552 (4.4)	2281 (6.5)	1878 (5.4)	824 (2.3)
35-39	526 (6.1)	416 (5.0)	557 (6.5)	457 (5.5)	210 (2.5)
40-44	92 (5.2)	69 (4.1)	121 (6.9)	94 (5.5)	55 (3.1)
45-49	20 (5.3)	11 (3.0)	25 (6.6)	15 (4.2)	16 (4.2)
50+	14 (7.9)	11 (6.4)	18 (10.2)	13 (7.6)	5 (2.8)
T-test	0.283	0.029	0.194	0.002	0.000
Chi-square trend	0.657	0.143	0.396	0.019	0.001

* For singleton births, n=88,858

TABLE III

The Impact of Paternal Age on Low Birthweight, Preterm Birth and Multiple Birth Among Women, Aged 25-29 and of First Parity, Alberta, 1990-1996 (N=36,234)

Paternal Age	< 2500 grams n (%)	< 37 weeks n (%)	Multiple Birth n (%)
≤ 19	1 (4.3)	2 (8.7)	0 (0.0)
20-24	126 (6.5)	140 (7.2)	16 (0.8)
25-29	1034 (5.8)	1205 (6.8)	183 (1.0)
30-34	817 (6.4)	974 (7.6)	176 (1.4)
35-39	212 (7.0)	222 (7.3)	44 (1.5)
40-44	31 (5.2)	40 (6.7)	8 (1.3)
45-49	3 (2.4)	6 (4.9)	3 (2.4)
50+	3 (4.5)	4 (6.1)	0 (0.0)
T-test	0.697	0.416	0.002
Chi-square trend	0.308	0.245	0.002

RESULTS

In this data set, the overall provincial rate of LBW between 1990 and 1996 was 6.3%, the rate of preterm birth was 7.3% and the rate of multiple birth was 2.2% (Table I). Within the provincial population of newborns (n=283,956), the risk of LBW, preterm birth and multiple birth was significantly increased in women aged 20 or younger and among those aged 40 or older (Table I). The lowest provincial rates of LBW and preterm birth occurred among women aged 25 to 29 at 5.8% and 6.8% respectively (Table I). Of the 283,956 births, maternal age data were available for all of them and paternal age was available for 259,903 (91.5%) births.

Among women aged 25 to 29 (n=90,948), the rate of LBW and preterm birth were not significantly impacted by paternal age (p=0.283 and 0.194 respectively) (Table II). Across paternal age groups, the rate of LBW ranged from 4.1% to 7.9%; the rate of preterm birth ranged from 5.5% to 10.2%. However, among singleton deliveries, there was a significant increased risk of LBW and preterm delivery when paternal age exceeded 50 years (p=0.029 and 0.002 respectively) (Table II).

Among women aged 25-29 and of first parity (n=36,234), the rate of LBW and

TABLE IV

Impact of Difference Between Paternal and Maternal Age on LBW, Preterm Birth and Multiple Birth, Among Women Aged 25-29, Alberta, 1990-1996 (n=90,741)

Age Difference (Paternal vs. Maternal)	< 2500 grams n (%)	< 37 weeks n (%)	Multiple Birth n (%)
5 to 9 years younger	51 (7.4)	65 (9.5)	15 (2.2)
4 to 0 years younger	942 (6.0)	1097 (7.0)	333 (2.1)
1 to 4 years older	2900 (5.5)	3435 (6.5)	1216 (2.3)
5 to 9 years older	985 (5.9)	1103 (6.6)	399 (2.4)
10 to 14 years older	189 (5.5)	210 (6.1)	84 (2.4)
15 or more years older	54 (5.2)	77 (7.4)	43 (4.2)
T-test	0.542	0.249	0.003
Chi-square trend	0.333	0.100	0.001

TABLE V

Impact of Difference Between Paternal and Maternal Age on Infant Outcomes LBW, Preterm Birth and Multiple Birth Between 1990-1996 in Alberta (n=259,903)

Age Difference (Paternal vs. Maternal)	< 2500 grams n (%)	< 37 weeks n (%)	Multiple Birth n (%)
10 years younger	54 (9.7)	59 (10.6)	6 (1.3)
5 to 9 years younger	417 (8.5)	500 (10.1)	148 (3.0)
4 to 0 years younger	3234 (6.4)	3797 (7.5)	1216 (2.4)
1 to 4 years older	8431 (5.8)	9979 (6.9)	3275 (2.3)
5 to 9 years older	2735 (6.1)	3115 (6.9)	1001 (2.2)
10 to 14 years older	647 (6.4)	728 (7.2)	210 (2.1)
15 or more years older	220 (6.9)	248 (7.8)	86 (2.7)
T-test	0.021	0.001	0.094
Chi-square trend	0.005	0.001	0.050

TABLE VI

Logistic Regression Analysis: The Relationship Between Maternal and Paternal Age and Birth Outcomes LBW, Preterm Birth and Multiple Birth, Within a Provincial Population (N=259,903) 1990-1996

	< 2500 grams		< 37 weeks		Multiple Birth	
Maternal Age	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
< 20	1.12	1.03, 1.23	1.11	1.02, 1.20	0.63	1.53, 0.76
20-24	1.07	1.02, 1.13	1.03	0.98, 1.08	0.86	0.79, 0.93
25-29	1.0		1.0		1.0	
30-34	1.09	1.04, 1.14	1.10	1.06, 1.15	1.12	1.05, 1.20
35+	1.27	1.19, 1.35	1.34	1.27, 1.42	1.12	1.01, 1.23
Paternal Age						
≤ 19	1.0		1.0		1.0	
20-24	0.84	0.74, 0.95	0.87	0.77, 0.97	1.12	0.84, 1.49
25-29	0.82	0.72, 0.93	0.82	0.73, 0.93	1.23	0.92, 1.64
30-34	0.77	0.67, 0.88	0.77	0.68, 0.87	1.25	0.93, 1.67
35-39	0.76	0.66, 0.87	0.75	0.66, 0.85	1.27	0.95, 1.71
40-44	0.79	0.68, 0.92	0.81	0.71, 0.93	1.23	0.90, 1.69
45-49	0.93	0.77, 1.13	0.88	0.74, 1.05	1.68	1.18, 2.34
50+	0.98	0.75-1.26	0.96	0.76, 1.21	0.90	0.53, 1.51

preterm birth was not significantly impacted by paternal age (p=0.697 and 0.416 respectively) (Table III). Across paternal age groups, the LBW rate ranged from 2.4% to 7.0%; the preterm birth rate ranges from 4.9% to 8.7%.

Among women aged 25 to 29, the risk of multiple birth with advanced paternal age and regardless of parity, was significantly increased (p=0.000 and 0.002 respectively) (Tables II and III). The risk of multiple birth seemed most elevated when paternal age was 15 or more years greater than maternal age (Table IV).

Within the newborn population (n=259,903), the risk of LBW and preterm birth was increased among couples where paternal age was 5 or more years less than maternal age (Table V). The risk of multiple birth, while significant, revealed a u-shaped curve of elevated risk among those couples with the greatest age difference.

Logistic regression (Table VI) revealed that, in the presence of maternal age, paternal age did not confer an increased risk of LBW, preterm birth and multiple birth. The maternal age variable was entered first into the regression. Paternal age was then added into the model to determine its independent effect on the outcome while controlling for maternal age effects (LBW, preterm delivery, and multiple birth). The effect of paternal age up to age 44, on risk of LBW and preterm delivery was relatively consistent and protective across age strata (i.e., confidence intervals are less than and exclude the value of one). The exception was the significant increase in multiple birth among those where paternal age was 45 to 49 years (odds ratio 1.68, 95% CI 1.18-2.34).

Results of multiple regression with paternal age and maternal age 25 to 29 revealed no effect on LBW outcome (p=0.469 and 0.213 respectively), no effect on preterm outcome (p=0.227 and 0.763 respectively), and a significant effect on multiple birth outcome (p=0.001 and 0.037 respectively).

CONCLUSIONS

There is a paucity of research on the impact of paternal age on LBW, preterm birth and multiple birth. This population-based analysis explored the relationship between paternal age and infant outcomes among women aged 25-29. Advanced paternal age may be associated with an independent increased risk of multiple birth among women aged 25-29 and an increased risk of LBW and preterm delivery among singleton deliveries when paternal age is 50 years or greater.

It is known that the risk of multiple birth increases with the use of fertility measures, including in vitro fertilization. Therefore, couples with unresolved infertility, potentially resulting from advanced paternal age, may be more likely to have increased risks of multiple births due to the potential use of in vitro fertilization (IVF).[30] Paternal age data are not maintained on the Regional Fertility Program Data Base, however 13.8% of mothers who deliver after in vitro fertilization are between the ages of 25 and 29 and within this maternal age group, 56.5% of infants are of multiple birth.[31] The data suggested that among women aged 25 to 29, the highest percentage of multiple births occurred when paternal age was 15 or more years older (4.2%) (Table V); therefore, it is plausible that these couples received infertility treatment due to advanced paternal age.

Logistic regression confirms that maternal age was a much stronger predictor of LBW and preterm delivery than paternal age. In fact, when maternal age was controlled for, paternal age was significant

only for an elevated risk of multiple birth among those where paternal age was 45 to 49 years. The effect of paternal age on risk of LBW, preterm delivery and multiple birth was relatively consistent across age strata. In this population, when maternal age was controlled for, paternal age conferred a protective effect. This finding has not been consistently noted in other studies. Indeed, Olsham et al. suggested that the risk of LBW and preterm delivery was not related to paternal age after adjustment for maternal race, gravidity, maternal smoking, marital status, maternal education and infant gender.[32] Other researchers have examined the effect of paternal age on risk of LBW and very LBW (<1500g), but have not included paternal age in their final model.[33] The variability in these findings may be related to our inability to control for multiple risk factors and indicates that further population-based research is necessary.

The reduction in number and the modification in mobility and morphology of spermatozoa increase after the age of 30, but particularly after the age of 55.[34] Paternal age has also been associated with an increase in risk of autosomal dominant mutations including achondroplasia, Apert Syndrome, Crouzon disease, Marfan's syndrome and retinoblastomas. Rates of these syndromes increase from 0.2 per 1000 births among fathers <29 years to 3.7 per 100 in fathers >45 years.[35-37] Additional research suggests a reduction in learning ability with increased paternal age.[38] These adverse infant outcomes are independent of maternal age and may have long-term consequences for infants. Paternal age may not be associated with LBW and preterm delivery, however there are age-related changes in men that may impact other birth outcomes as described above. Therefore, there is a need for increased awareness of these syndromes and diseases with advanced paternal age when planning families.

In this data set, it was not possible to identify IVF infants to more closely examine the relationship between paternal age, IVF, multiple birth and infant outcome. Including singletons and multiple births in the analysis of risk for LBW and preterm birth biased findings towards the null. Excluding multiple births from the analysis of LBW and preterm delivery, the data reveal that, among singleton births, paternal age in excess of 50 years increased the risk of LBW and preterm birth.

The simple analytical strategy employed in this study was used to determine the impact of paternal age on birth outcomes among a low risk population. The advantage of this analysis was the inclusion of LBW and preterm infants, and the large sample size. As well, the analysis specifically looked at the effects of paternal age among those women who were at the lowest risk of poor infant outcomes (i.e., women aged 25-29), and to control for parity. The effect of age difference among mother and father on birth outcomes was also determined among this low risk population of mothers. The analysis led us to hypothesize about reasons for increased multiple births among this low risk population, including possible increased IVF treatment due to advanced paternal age and large age differences within couples.

The finding that there was an overall increased risk of LBW and preterm birth among couples where paternal age is 5 or more years younger than maternal age likely reflected more advanced maternal age in these cases. The impact of maternal age on an elevated risk of LBW, preterm delivery and multiple birth has been described.[39]

These findings are generalizable only to those ultimately able to conceive and the proportion of couples with unresolved infertility would not be included in this analysis. Alternatively, the recent availability of in vitro fertilization and artificial insemination, including its success rates of approximately 50% in Alberta, increase the likelihood that those with unresolved male infertility may obtain treatment. Finally, these findings may reflect our current medical practices and environment and should be taken within that context.

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Received: January 25, 2002
Accepted: August 20, 2002

RÉSUMÉ

Objectif : Déterminer si l'âge paternel accroît le risque d'insuffisance de poids à la naissance (<2500 g, IPN), de naissance avant terme (<37 semaines de gestation) et d'accouchement multiple chez les mères dont l'âge n'est pas une variable prédictive de risque élevé.

Conception/méthode : Les données démographiques sur l'issue de la grossesse, l'âge maternel et l'âge paternel provenaient du ministère albertain de la Santé et du Bien-être pour toutes les naissances de 1990 à 1996.

Résultats : Pour les femmes de 25 à 29 ans, primipares ou non, il n'existait aucune relation linéaire entre l'âge paternel et la naissance avant terme ou l'IPN. Toutefois, les taux d'accouchement multiple augmentaient avec l'âge paternel ($p<0,01$). Pour les accouchements simples, un âge paternel avancé (>50 ans) augmentait le risque d'IPN et de naissance avant terme ($p\leq0,05$).

Conclusion : L'âge paternel n'est pas un facteur de risque d'IPN ou d'accouchement prématuré chez les femmes à risque modéré. Le risque accru d'accouchement multiple avec la hausse de l'âge paternel, que la mère soit primipare ou non, doit être confirmé par des recherches dans d'autres populations.