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Slow Twin Conception at First Birth and Subsequent Maternal Twin Proneness in a Natural Fertility Population*

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Abstract. To study whether apparently more fecund women having delivered twins at first birth have traits of higher twin-proneness, we performed a retrospective cohort study on population-based historical vital records of the 17-18th century French Canadian immigrants and their descendants under natural fertility conditions. Among 24896 mothers who had at least one child, 248 had twin maternities at their first birth (twinning rate = 1.0%). Among 21508 mothers with a valid marriage-first birth interval, twinning rate was 0.97% among prompt conceptions (7.0-11.0 months), with a particularly high rate at the interval of 7.0-8.0 months (2.2%). Marriages in August-October resulted in a higher twinning rate particularly for the slow conceptions than those in the other seasons. Promptly-conceived mothers of twins at the first delivery may seem to have higher fecundity, but subsequent births from these mothers (n = 88) show a lower twinning rate (1.7%) particularly at younger maternal age than from the other mothers who had slowly conceived twins at their first birth (n = 112). The latter show a 4.5% twinning rate as a whole among their second or later births. So-called twin-proneness of a mother, whether genetic or acquired, was not connected to higher conception rate of twin's mothers immediately after marriage. Reduced fecundity, which may have been imposed by some environmental factors, could raise the chance of twinning.

Key words: Twinning, Fecundity, Natural fertility, Subfertility, First birth interval, Genetics, Twin-proneness, Season

INTRODUCTION

Using natural fertility data it has been reported a larger family size for parents of twins than for mothers of singletons only [25]. The same dataset indicated, however, that twin maternities tended to be preceded by an unusually long birth interval [24]. The apparent

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high fertility for parents of twins was shown to have been caused by a bias of selecting mothers who had continued reproduction at higher ages [1]. The well-known fact that the twinning rate peaks at the maternal age of 35-39 years [3, 4] caused the apparently higher fertility among the mothers of twins, observed retrospectively. Ideally, to assess the fecundity of a couple, we need data on fecundability, or the probability of successful conception at one given unprotected menstrual cycle. Actually, the data available are limited particularly for the contemporary population, and thus relationship between twin-proneness of a mother and her fecundity is still a matter of controversy.

Some reports seem to suggest higher fecundity for mothers of twins. Unlike monozygotic (MZ) twinning, dizygotic (DZ) twinning has been reported to vary to a great extent by many factors, such as race, maternal age, birth order, season and geographical location [4]. A study [13] showed ultrasonographic evidence that mothers who had spontaneously conceived more than one set of DZ twins experienced multiple ovulation at subsequent normal menstrual cycles. Although we can not directly associate this result with higher fecundity, the DZ-bearing mothers seem to have a specific biological background for twin maternity. Some studies have suggested that twin-bearing mothers are more fecund on the basis of an earlier peak of twin than singleton births in the U.S. after the return of husbands from World War II [2] and of a higher twinning rate among illegitimate births [8].

But there is another line of evidence apparently independent from the above hypothesis. It has been reported, using data from historical New England, that twin maternities were concentrated at the last birth of each family size; thus showing that a decline in fecundity, even at younger maternal ages, facilitates twin maternities [14]. This hypothesis has been supported by the observation of prolonged birth intervals immediately before the index twin maternity, particularly for mothers in their early thirties, among other natural fertility populations. It has been also hypothesized lower fecundity for mothers of twins, having attributed the difference to over-ripeness ovopathy [10].

Are there two independent causes that facilitate DZ twinning, one related to higher fecundity and the other to lower fecundity? It has been suggested that DZ-twin-proneness is determined by a possibly recessive gene [4], though the penetrance of the gene is surely far less than one hundred percent. If some mothers are genetically predisposed to conceive twins, we could regard the mothers who actually delivered twins to have the traits. If some mothers have genetic traits of twin-proneness and if these traits are related to high fecundity, then we would expect earlier conception at first birth for twin maternities and higher twinning in subsequent births.

Under conditions of natural fertility, where couples practise no contraception, marriage marks the beginning of exposure to the risk of conceiving when premarital sexual activity is negligible. The interval between it and the first birth then measures the time necessary to succeed in both conceiving and carrying the product to term. Although the two cannot be distinguished, the interval can be considered to reflect fecundity. In this paper, we test the above hypothesis, focusing on women who delivered twins at the first birth and separating them according to the promptness of the first successful conception.

MATERIALS AND METHODS

The data analyzed in the present study were extracted from a databank for the French-Canadian population of the 17th and 18th centuries. This computerized database has

been created and is now being expanded within the Programme de recherche en démographie historique at the University of Montréal, Canada. The details of this database have been described elsewhere [11]. Briefly, it is a population-based database covering births, marriages, deaths from 1621, the early days of immigration from France, to the year 1765 when French rule ended. The population is known to have been highly fertile without any evidence of artificial contraception [5] and thus to have functioned under natural fertility. The information is available both at the individual and family levels. The births in this database can be basically considered as live births, although they may include sporadic cases of stillbirths which were reported by midwives as immediately-deceased live births in the death certificate.

For the present analysis, a set of variables were extracted from the database on a family basis: the women who married and had at least one child were used (n = 24896). The information for the mothers was further extracted from the database, including all the births from the mothers, even if they re-married. The variables used in the present analysis were the plurality of the first maternity, marriage and first birth dates, maternal age and plurality for second or later maternities. The first birth interval, or the marriage-first birth interval, was calculated in days as long as valid dates were available. Cases without valid information on the dates of marriage or first birth (n = 2001, 8.0%) were treated as cases with a missing interval and excluded from the present analysis. The interval calculated in days for the remaining 22895 mothers was further divided by 30 to show the length of the interval in months. Because the length of gestational period is shorter on average from twin maternities, we must adjust the apparent promptness of conception for the mothers of twins. Because we do not know individual gestational lengths, we systematically add 19 days [2] to each first birth interval calculated for the twin maternities. We defined, after the adjustment, the prompt conceptors as having from 7.0 to 11.0 months ("prompt mothers"), and the others as the slow conceptors ("slow mothers"). Some mothers (n = 1387; 6.1%) had very short, 7.0 months or less, first birth interval; this group certainly selects cases with premarital sexual relationship. These mothers were separately handled in the present study.

As observation ends in 1765, reproductive histories are truncated for the later marriages. To overcome this problem, we calculated agespecific (5 year-grouped) twinning rates, in addition to the whole rate on the available data, when comparing groups of mothers.

All works of tabulation and statistical analysis were done using SAS on a Sun workstation at Teikyo University, Tokyo. We utilized SAS date functions in calculating intervals, and mainly used the *freq* procedure to crosstabulate the data and compute the statistics.

RESULTS

Among 24896 mothers who had at least one child, 248 experienced twin maternities at their first birth (twinning rate = 1.0%). Among 21512 mothers with a valid marriage-first birth interval the twinning rate was 0.93%, and the rate varied to some extent according to the marriage-first birth interval (Table 1). The highest twinning rate was observed at the shortest interval: 2.2% at 7.0-8.0 months. But the twinning rate for the other interval

Table 1 - Twinning rate at first birth according to marriage-first birth interval

Marriage-first birth interval (months)	Number of maternities			Twinning rate (%)
	Singleton	Twin	Total	
(-7.0	1.373	10	1.383	0.7)*
<Promptly-conceived mothers>**				
7.0-8.0	306	7	313	2.2***
8.0-9.0	1.337	13	1.350	1.0
9.0-10.0	4.090	41	4.131	1.0
10.0-11.0	3.232	27	3.259	0.8
Subtotal	8.965	88	9.053	0.97
<Slowly-conceived mothers>**				
11.0-12.0	2.198	22	2.220	1.0
12.0-24.0	7.546	64	7.610	0.8
24.0+	2.603	26	2.629	1.0
Subtotal	12.347	112	12.459	0.90
Total	21.312	200	21.512	0.93

* excluded from the total line.

** Twining rates between the two groups of mothers were not different significantly (p = 0.581 by Fisher's 2-tailed exact test).

*** This group shows a significantly higher twinning rate than the rest (p = 0.028 by Fisher's 2-tailed exacttest).

Table 2 - Effect of marriage season and marriage-first birth interval on twinning rate at first birth

Marriage-first birth interval (months)	Marriage season					Probability p-value*
	Feb-Apr	May-Jul	Aug-Oct	Nov-Jan	Total	
	Twin/All	Twin/All	Twin/All	Twin/All	Twin/All	
Prompt	25/2353	12/1423	23/1779	28/3498	88/9053	0.332
(7.0-11.0)	(1.1%)	(0.8%)	(1.3%)	(0.8%)	(0.97%)	
Slow	22/3317	10/1867	33/2731	47/4544	112/12459	0.033**
(11.0+)	(0.7%)	(0.5%)	(1.2%)	(1.0%)	(0.90%)	
Total	47/5670	22/3290	56/4510	75/8042	200/21512	0.050
	(0.81%)	(0.67%)	(1.20%)	(0.92%)	(0.93%)	

* chi-squared test for the uniformity of four seasons (df = 3).

** $p < 0.05$.

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Table 3 - Outcomes of 2nd or later births to mothers bearing twins at first birth

Marriage-1st birth	7.0-11.0 months (Prompt Mothers)	11.0 months + (Slow Mothers)	p-value*
Maternal age	Twin/All	Twin/All	
-19 (years)	0/ 37	1/ 16	0.302
20-24	0/ 74	4/ 70	0.053
25-29	0/122	6/135	0.031**
30-34	2/125	6/126	0.281
35-39	3/88	4/101	1.000
40-44	3/37	1/35	0.615
45-49	0/0	0/2	—
Age total	8/483 (1.7%)	22/485 (4.5%)	
Number of mothers	88	112 ***	

* Difference between the prompt and the slow mothers, assessed by Fisher's 2-tailed exact test.

** $p < 0.05$.

*** The number of births per mother is affected by the truncated observation.

groups were rather stable, ranging from 0.8% to 1.0%. When we dichotomized the mothers into two groups, "prompt mothers" and "slow mothers", the prompt mothers had a higher twinning rate, but the difference between the two groups was not significant ($p = 0.581$ by Fisher's 2-tailed exact test).

Marriage season influenced the twinning rate at the first birth. As shown in Table 2, the August-October season had a tendency of a higher twinning rate (1.2% in total, $p = 0.050$ for four seasons), although a statistically significant difference was more clearly seen among the slow mothers (1.2%, $p = 0.033$ for four seasons).

We calculated age-specific twinning rates for the second or later births of mothers who had delivered twins at their first birth (Table 3). The prompt mothers (n=88) had only 8 sets of twins among 483 subsequent maternities (1.7%), whereas the slow mothers experienced a higher twining rate (22 sets of twins among 485 maternities, 4.5%). Differences between the two groups of age-specific twinning rates were statistically significant at the maternal age of 25-29 years ($p = 0.031$ by Fisher's 2-tailed exact test), and relatively higher twinning rates for the slow mothers were observed particularly at younger maternal ages up to 35 years of age.

DISCUSSION

A study reviewed the issue of twinning and fertility, concluding that DZ twinning may be influenced by genetic variation in maternal physiology, by variation in diet and health, and even by psychological stimulation to gonadotropin secretion, particularly for

twin births among early conceptions or from illegitimate unions [1]. Concluding remarks were: "There is no direct evidence that twin-prone women conceive more readily than other women, but when they happen to conceive promptly they are apparently more likely to conceive twins than when they happen to conceive late". Present data suggest the excess of twins among earliest conceptions in the historical French-Canadian population (Table 1).

Although the present paper has not analyzed intergenerational tendencies of twinning, the present results seem to indicate more contribution of environmental factors to the twinning. As shown in Table 3, twin-prone mothers, regardless whether genetically determined or not, are *not* the early conceptors at their first birth. These prompt, or more fecund, mothers at their first twin birth experienced a rather lower twinning rate among their subsequent maternities, and a higher recurrent twinning was seen only for the slow mothers. The prompt mothers may have experienced a higher than usual gonadotropin surge and/or follicular function before conception, possibly by some psychological stimulation [1], but this phenomenon was temporary and did not seem to be long-lasting for the rest of the mothers' lives. This may rebut the genetic background for mothers having delivered twins at their first confinement.

Then, is twin-proneness among the slow mothers genetically determined? A recent study [7] using five restriction fragment length polymorphisms in four hormone genes found no significant differences between DZ twin mothers and controls. Twin-proneness among the slow mothers in the present study, even if fundamentally under the influence of unspecified gene(s), also seems to have been expressed in response to some seasonal environmental factors. Among the slow mothers, those who married in the August-October season showed a significantly higher twinning rate than the others (Table 2). Although this might be explained by differential proportions of surviving twin conceptions according to marriage season, it is also possible that the incidence of twin conception itself was affected by season. If this difference is real, it cannot be explained by a static genetic model.

It has been suggested that the birth season of a female herself could affect her later reproductive outcomes, such as the season of birth of her offspring [17, 19], sex ratio at birth [16] and twinning [15]. These apparently "astrological" phenomena have been discussed on the ground of some seasonal, possibly microbial, factors having acted during pregnancy and having left the fetuses with long-lasting effects even long after birth. For similar phenomena, Jongbloet has suggested another hypothesis with the idea of seasonal preovulatory over-ripeness ovopathy [10]. We have so far no materialistic evidence for the phenomena, but these observations suggest the importance of the effects of seasonal factors on the intrauterine environment.

The present results suggest that twin maternity, probably the DZ one in particular, is associated with a drop in maternal fecundity under natural fertility conditions. We are not to deny the genetic tendency of twin-proneness [4], and it seems reasonable to hypothesize some genes which determine the levels of gonadotropin and/or inhibin secretion. However, the present finding suggests that non-genetic factors are also involved in the mechanism of actually-observed twinning. Seasonality has been reported for twin births. Environmental factors which exist seasonally and change their effects secularly can possibly trigger twin maternities. In this sense, it is interesting that environmental pollution due to incinerators may have elevated the local twinning rate [12]. However,

because the seasonality of twinning was recorded even in a pre-modern era [20, 22], the triggers for twinning should not solely be attributed to environmental pollutants in the 20th century. The "last-birth phenomenon" where twin births are more concentrated at the last birth order of families for each family size [14], has been interpreted to mean that subfertility, usually unnoticed and possibly triggered by some infectious agents, is likely to be accompanied with multiple ovulation through impaired regulatory function of the human reproductive system. Recent reports on seasonal variation in the incidence of vanishing twins [18] and early pregnancy loss before 42 days from the onset of the last menstrual period [23] may suggest that we are still under the influence of seasonal environmental factors in spite of the present de-seasonalized living conditions due to the development of public health facilities and air-conditioning systems. Seasonal variation in the success rate of artificial insemination, a trough in around May [21], also indicates the contribution of seasonal factors other than human sexual behavior.

If the drop in fecundity elevates the possibility of twin maternity, this could shed some light on the higher incidence of twinning among the infertile women treated with fertility drugs. Although the higher incidence of multiple pregnancy seems reasonably correlated with the use of drugs, these women may have been more at risk of multiple ovulation than the other fertile women in the first place. Reduction of the incidence of iatrogenic multiple pregnancies is wanted [9]. Although effort has been made to reduce the chance of unwanted multiple pregnancies with a conservative treatment protocol with human menopausal gonadotropins, the goal does not seem to have been attained [6]. If the conservative treatment protocol has failed to reduce multiple births, we have to consider the possibility that the infertile women, *per se*, are at a higher risk of multiple ovulation by any stimulation.

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