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## Maternal Age and Parity as Predictors of Human Twinning

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**Abstract.** A case-control study was conducted to evaluate the association between maternal age and parity and dizygotic (DZ) and monozygotic (MZ) twinning, respectively. Mothers of all twins born alive in Denmark in 1984 or 1985 were included into the study as cases, and a random sample of mothers of singletons were controls. Data on maternal age at delivery and number of previous births were collected from the Danish Medical Birth Register. By means of logistic regression analysis, a significant and positive association was found between maternal age and DZ twinning, and a significant and negative association between parity and MZ twinning. No association was found for parity and DZ twinning, nor for maternal age and MZ twinning. The study suggests that human MZ twinning has predictors too, as has DZ twinning. The finding has implications for zygosity classification in future twin research.

**Key words:** Maternal age, Parity, Twinning

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### INTRODUCTION

When searching for possible etiological factors leading to twin birth, the association between maternal age and parity has been known for a long time [6]. Many studies have reported increasing twinning rates with maternal age up to a maximum at 35 to 39 years and gradual rises for twinning rates with birth order independent of maternal age [1,3,7,9,11,12]. The increase in twinning rates with maternal age and parity has been found to be due to increases in dizygotic (DZ) twinning rates only, monozygotic (MZ) twinning rates being fairly constant. Many studies have categorized the twins into DZ and MZ pairs based on the sex of the twins. This may cause a substantial amount of misclassification of same-sexed DZ twins into the group of MZ twins. This could possibly eliminate an existing effect of maternal age and parity if this was in the opposite direction of the association found for DZ twins.

The purpose of the present study has been to reevaluate the association between maternal age and parity for DZ as well as MZ twinning in a society where parity no longer reaches the levels mentioned in previous studies. Moreover, a zygosity classification has been used associated with a very little amount of misclassification, which gives a greater power to reveal a possible association for MZ twinning if it exists.

## MATERIAL AND METHODS

### Study Subjects

The information concerning the present case-control study was gathered from the Danish Medical Birth Register. Mothers of all twins born alive in Denmark in 1984 and 1985 were included as cases, and controls were mothers of a random sample of approximately 1.5% of singleton infants born in the same time period. The twins were split up into DZ and MZ pairs according to the similarity method [4]. Data on the similarity of the twins were gathered using a questionnaire which was sent out between September 1985 and August 1986. The response rate was 89% for the twin mothers and 80% for the control mothers. The overall response rate was 83%. The zygosity of the twins of the non-responders (11%) could not be determined. The other twins were classified as DZ in case of different sex or of same sex but different hair or eye colour. Same-sexed twins were regarded MZ if they had the same hair and eye colour, if they were strikingly similar in appearance (as two peas in a pod), and if telling them apart had caused problems for family and friends. The sensitivity (test for likeness) of this method, which has been evaluated on children of similar age, was 94% and the specificity (test for unlikeness) was 100% [4]. By this method, 402 pairs were classified as DZ, 252 as MZ and 349 could not be classified.

All mothers treated with ovulation inducing hormones were excluded from the study.

### Analysis

The data have been analysed using logistic regression analysis [2]. The dependent variable for the analytic approaches were DZ and MZ twinning, respectively. The two variables, maternal age (as 5-year truncated age groups) and parity (as a continuous variable or truncated at different levels) were included into the model (Table 1). Maternal age and parity were included into the logistic regression models simultaneously, which implies that all results have been adjusted for confounding caused by age or parity, respectively.

## RESULTS

The characteristics of the study population are listed in Table 1. The mean maternal age and parity of the different study groups are listed in Table 2. An analysis of variance revealed a significant difference between DZ mothers and control mothers for maternal

**Table 1 - Characteristics of the study population**

	N	%
<b>Study groups</b>		
Mothers of DZ twins	402	15.4
Mothers of MZ twins	252	9.7
Mothers of unclassifiable twins	349	13.4
Mothers of singleton infants	1606	61.5
<b>Maternal age groups (yr)</b>		
19 or less	81	3.1
20 - 24	657	25.2
25 - 29	1022	39.2
30 - 34	609	23.3
35 or more	240	9.2
<b>Parity groups (no. of previous births)</b>		
0	1130	43.3
1 or more	1479	56.7

age ( $F = 19.25$ ,  $p = 0.00001$ ) and parity ( $F = 6.10$ ,  $p = 0.01$ ) and for MZ mothers and control mothers for parity ( $F = 6.25$ ,  $p = 0.01$ ), but not for age ( $F = 2.35$ ,  $p = 0.13$ ). Table 2 shows that the mothers of DZ twins have the highest mean age, and mothers of MZ twins the lowest. This pattern applies to parity, too. The mean values have not been controlled for age and parity, respectively, in contradiction to what has been done in the logistic regression analysis.

The results of the logistic regression analysis are shown in Table 3. The odds ratio (OR) for DZ twinning is significantly and positively associated with maternal age, but not with parity. The opposite was found for MZ twinning: no significant association between MZ twinning and maternal age, but a significant and negative association between

**Table 2 - Mean values for maternal age and parity and 95% confidence intervals (CI) for the means for the study groups**

Study groups	Age years		Parity	
	Mean	95% CI	Mean	95% CI
Mothers of DZ twins	28.4	28.0-28.9	0.91	0.82-1.00
Mothers of MZ twins	26.7	26.2-27.3	0.63	0.53-0.74
Mothers of singletons	27.2	27.0-27.5	0.79	0.74-0.83

**Table 3 - Odds ratios (OR) and their 95% confidence intervals (CI) for DZ twinning vs controls and for MZ twinning vs controls for maternal age and parity**

	DZ twinning		MZ twinning	
	OR	95% CI	OR	95% CI
Age	1.24	1.10-1.41	0.96	0.82-1.12
Parity (continuous) <sup>a</sup>	1.03	0.90-1.18	0.83	0.69-1.00
Parity (truncated) <sup>b</sup>	1.15	0.90-1.49	0.73	0.54-0.99

<sup>a</sup> The values of parity have the range 0-8 (previous births)

<sup>b</sup> Truncated as no previous birth or one or more previous births.

parity and MZ twinning, both when parity was analysed as a continuous variable and at different truncation levels.

The association between DZ twinning and maternal age was examined in more detail and a significant association with age (OR = 0.90, 95% confidence intervals (CI) = 0.82-0.99) was found. The inclusion of age into the model improved the fit of the model:  $G = 5.72$ ,  $df = 1$ . This implies that the association between DZ twinning and maternal age is not linear, but that it follows a hyperboloid curve with an age maximum in DZ twinning rate. For MZ twinning, no significant association with parity (OR = 1.05, 95%CI = 0.97-1.13) was found. This implies that the best model of the association between MZ twinning and parity is a linear one.

## DISCUSSION

The finding of the present study of a positive association between DZ twinning and maternal age is in accordance with the literature [1,3,7,9,11,12]. This accounts, too, for the finding that maternal age constitutes the best fit to the model. The implication of the latter finding is that the twinning rate peaks at some age levels which have been shown to be between 35 and 39 years.

The finding of no association between DZ twinning and parity is not in concordance with the literature, although a few authors previously have failed to demonstrate this association [5,8,10]. The conclusion is drawn from the logistic regression analysis where the association between DZ twinning and parity has been adjusted for maternal age. The reason that a significant difference was found when comparing the mean values of parity for DZ and control mothers is a matter of confounding by age. For these mothers, a significant interaction between age and parity (OR = 0.90, 95% CI = 0.79 - 1.00) was found.

The lack of an association between DZ twinning and parity might be related to the fact that the mean number of pregnancies for women in our society does not reach the same high level as mentioned in previous studies. As can be seen from Table 1, the mean number of previous births for the women included in the present study was 0.8 (prior

to the index birth). Pregnancies in the present Danish society are, to a great extent, planned (3.7% unplanned pregnancies in the present study), and fertility is effectively controlled by contraception and induced abortions. So, the data, as we see them here, reflect the restrained fertility of the population and only to a minor degree the true biological potential.

A slight increase in MZ twinning rate with maternal age has been shown previously [3]. Other studies have not revealed any association between MZ twinning and maternal age or parity. So, the finding of a negative association between MZ twinning and parity has not been demonstrated earlier. The reason for this previous lack of association might be related to the method of zygosity classification which has been widely used, namely, the one based only on the sex of the twins (not the Weinberg method). This gives a DZ group with no misclassification because it is based on opposite-sexed twins only. All same-sexed twins constitute the MZ group, and this includes a considerable amount of misclassified DZ pairs. This misclassification will tend to adjust for differences which deviate in opposite directions for MZ and DZ twinning. The number of misclassified pairs in the present study is presumably small, based on the high validity of the method.

The biological background of the results of the present study is difficult to assess, but DZ and MZ twinning are, indeed, two different biological phenomena. They should not be regarded as a unity of twins or of same-sexed twins because this might tend to remove existing differences. The finding of a significant and negative association between MZ twinning and parity is new and may imply that there are predictors of human MZ twinning, too.

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