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The Epidemiology of Multiple Pregnancies

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Abstract. Over the last decades the frequency of multiple births has been on the decline in most developed countries. This trend, however, has been restricted to dizygotic twins, while monozygotic rates have remained stable or risen slowly. In more recent years, however, the fall in multiple dizygotic birth rates has ceased and a slight increase is observed. This trend and the increased frequency of triplets or higher-order births, registered from the early 1980s onwards, are essentially related to treatments for infertility. No single risk factor, such as maternal age, parity, oral contraceptive use, or declining fertility rates can explain the overall declining trends. In this paper we review the descriptive epidemiology and the main risk factors for multiple pregnancies.

Key words: Epidemiology, Risk factors, Multiple pregnancies

INTRODUCTION

The decline in the frequency of multiple births in most developed countries over the last decades has been restricted to dizygotic (DZ) twins, while monozygotic (MZ) rates have remained stable or risen slowly [1,2,5,6,10,11]. Data in more recent years from the United Kingdom, Denmark and Canada have suggested that the decrease in multiple DZ birth rates has stopped, and, if anything, a slight increase was observed, while triplet rates have markedly risen from the early 1980s onwards [3,7,12].

These simple epidemiological observations have suggested that changes in lifestyle and/or reproductive habits in the last decades have markedly influenced DZ twinning rates. In this paper we review the descriptive epidemiology and main risk factors for multiple pregnancy. Special focus is given to the trends in multiple pregnancy rates in Italy.

Geographic and temporal trends in Italy and other countries

In Italy between 1955 and 1985 the frequency of multiple births declined from 12.6/1000 deliveries (1 every 79 deliveries) to 9.4/1000 deliveries (1 every 106 deliveries) [17]. This downward trend was constant until the early 1970s when rates tended to level off and then to slightly increase again in the early 1980s (Fig. 1). In the late 1980s, however, an increasing trend was observed, and in 1989 the rate of multiple births was 10.4/1000 deliveries. However, these trends were largely attributable to DZ rates as MZ births were relatively constant over the considered period (Fig. 2). The proportion of triplets or higher order births on the total of multiple births was constant from 1955 to the late 1970s, after which it rose markedly, being 1:99 in the quinquennium 1955-1959, 1:103 in 1975-1979, 1:70 in 1980-1983 and 1:38 in 1989 (Tab. 1).

Similar trends in absolute and relative terms have been reported from North European and American countries [3,7,12,14]. For example, in England the frequency of multiple pregnancies was 12.2/1000 pregnancies in 1956-1959, declining to 9.7 in 1976-1980, but increasing to 10.2 in 1983-1985, with an estimated MZ rate of about 3.5-3.8/1000 pregnancies over the entire period 1955-1985 [3].

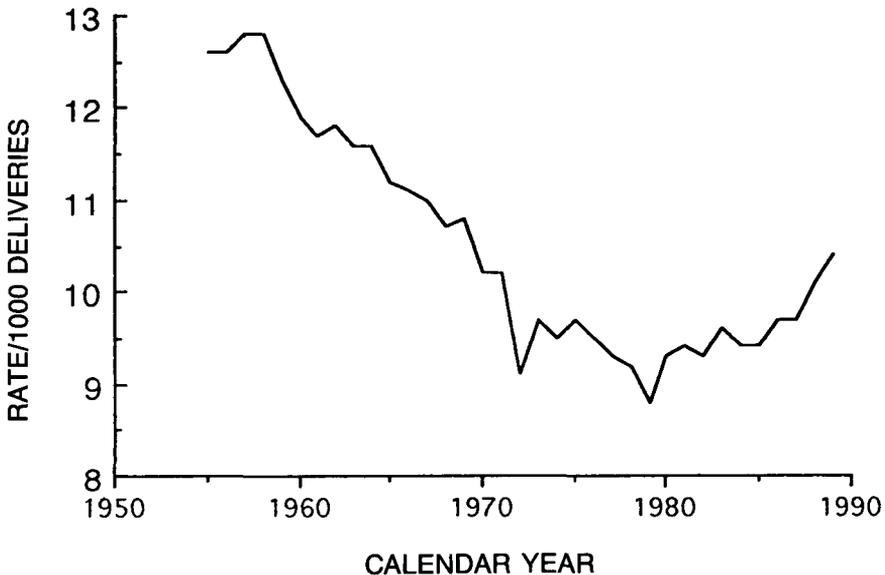


Fig. 1. Trend in multiple pregnancy rates in Italy, 1955-1989.

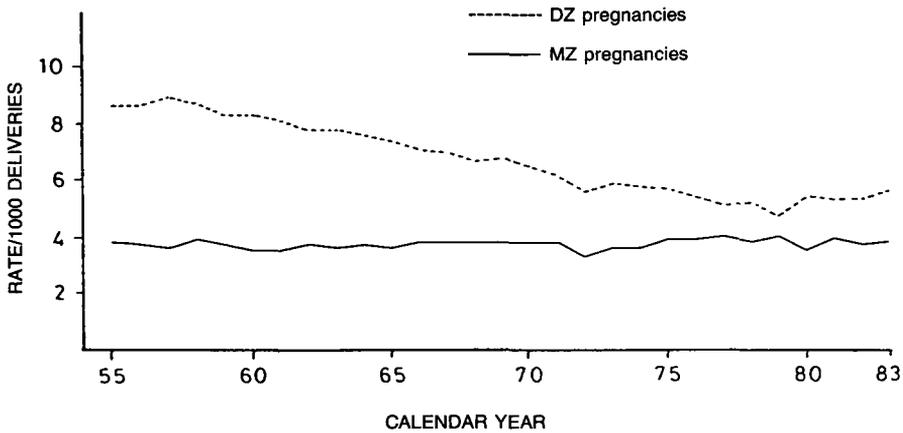


Fig. 2. Trend in dizygotic and monozygotic twinning in Italy, 1955-1983.

Table 1 - Trends in multiple birth rates in Italy, 1955-1989

	Calendar period						1989
	1955-59	1960-64	1965-69	1970-74	1975-79	1980-83	
Multiple birth rates/ 1000 pregnancies	12.6	11.8	11.0	9.8	9.3	9.4	9.6
DZ rates/ 1000 pregnancies	8.8	8.1	7.2	6.1	5.4	5.4	n.a.
Triplets or higher- order birth rates/ 1000 pregnancies	0.13	0.12	0.11	0.09	0.09	0.13	0.27

n.a. = not available

RISK FACTORS

Age

As for most obstetric conditions, “advanced” maternal age is a prime risk factor for multiple pregnancy. Multiple birth rates in various strata of maternal age in Italy are presented in Table 2. The highest rates were in the 35-39 years age group, but flattened out in the subsequent age strata. The differences within the various age groups were more marked for DZ multiple pregnancies: in 35-39-year-old women rates were more than threefold higher than in those aged 20 or less. Monozygotic rates were slightly upward till age 35-39, but the differences were limited [17]. These findings are common in various populations [3].

No obvious reason has been identified to explain the decreasing rates of dizygotic births found in women of 40 years or more. Selective mechanisms, such as, the greater

Table 2 - Multiple birth rates according to maternal age and zygosity in Italy, 1980-1983

Maternal age	Total number of deliveries	Multiple births/1000 deliveries	
		DZ	MZ
≤ 19	159.069	2.5	3.6
20-24	747.066	4.2	3.6
25-26	823.302	5.4	4.2
30-34	505.582	7.3	4.1
35-39	185.916	8.1	4.5
40-44	43.853	6.0	3.8
≥ 45	3.177	n.e.*	4.7**

* Not estimated (no unlike-sex multiple birth was observed in this age strata in the considered period)

** Probably including some like-sex dizygotic pregnancies.

frequency of abortions in multiple pregnancies in older women, and genetic and environmental factors can all be suspected, but these hypotheses are merely speculative.

Socioeconomic factors

A higher frequency of multiple pregnancies in the lower social classes has been reported in studies conducted in Nigeria and Scotland and reported also among illegitimate maternities [8,16]. It has been suggested that these differences might be explained in terms of the different reproductive or dietary habits of women in the lower social classes, but this relation between social class and multiple pregnancy has not been consistently reported. For example, in the United Kingdom multiple birth rates were comparable in the different social classes [15].

Reproductive history

Clinical observations have suggested that high parity is associated with an increased risk of multiple DZ pregnancies. For example, a higher incidence of multiple pregnancies associated with parity has been shown in a comparative study of multiparous women conducted in India and Scotland [13], however, these findings are far from consistent [18]. The relationship between parity and multiple pregnancy can be interpreted in terms of non-adjustment or incomplete adjustment for the confounding effect of maternal age.

A potential association between spontaneous abortions and multiple pregnancies has been suggested on the basis of a geographical correlation observed between larger numbers of spontaneous abortions and smaller numbers of twin births [24], but the scanty data available from formal epidemiological studies have not confirmed this suggestion [18] and, in the absence of a biological interpretation, this observation necessarily remains speculative.

Oral contraceptive use

It has been suggested that oral contraceptive use may increase the risk of multiple births. Terminating oral contraceptive use might determine an increase in the gonadotropin level which, in turn, causes a multiple ovulation. An analysis conducted in Connecticut found that the risk of multiple births was about three times higher in women conceiving within two months of terminating oral contraceptive use [4]. Similar evidence emerged from a postal survey carried out in the United States [19] and from the Royal College of General Practitioners' Oral Contraceptive Study conducted in England in 1974. However, no relationship between oral contraceptive use and multiple births was found in another study conducted in the United Kingdom [22] and an inverse association was reported from a French study [9].

Family history of multiple pregnancies

A family history of multiple pregnancies is traditionally considered a "risk factor" for twinning. This clinical observation has been confirmed in epidemiological studies [18]. The risk of multiple births is roughly doubled in women whose mother and sisters have had twins, and this risk seems to be greater for monozygotic pregnancies than dizygotic ones. This relationship may be, in part, overestimated. In fact, in epidemiology studies it is extremely difficult to exclude the possibility of memory bias; in other words, women who have had twins may recall a family history of multiple pregnancies more easily than women who have had single pregnancies.

Other factors

It has been suggested that mothers of twins are of heavier weight and have an earlier menarche and menopause [23]. These findings have been discussed in terms of different gonadotropin level patterns in overweight women and their interaction with menstrual characteristics. However, the evidence available on this issue is largely inconsistent. Likewise, in some recent studies on the risk of multiple pregnancy, data obtained on the role of dietary habits and of a lower mean number of spermatozoas is both poor and inconsistent.

CONCLUSIONS

In later years, epidemiology has offered some of the most interesting findings to help clarify the mechanisms regulating the development of multiple pregnancies. The marked decreasing trends observed in DZ pregnancy rates up until the early 1980s suggest that environmental factors play a role in determining this condition. On the contrary, the constant frequency of MZ pregnancies over time and in different geographic areas suggests that monozygotic pregnancies are largely determined by genetic mechanisms. The increase in triplets or higher order births registered from the early 1980s onwards is es-

entially related to treatments for infertility [20,21]. This has probably also had some impact, although difficult to quantify, on the changed trends in twin births as well.

No single risk factor, such as maternal age, parity, oral contraceptive use, or declining fertility rates explain the trends observed and these, therefore, can only tentatively be related to lifestyle habit changes.

In the near future, epidemiological research will be obliged to activate etiological studies on the risk factors for this condition. In terms of descriptive epidemiology, it is important to continue monitoring the frequency of the condition in order to understand if, for example, the "flattening" observed in the early 1980s was effectively the beginning of a new trend. Finally, it would be interesting to quantify the effect of infertility treatments on the frequency of multiple dizygotic pregnancies.

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