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Dizygotic to monozygotic twinning ratio at The Royal Women's Hospital, Melbourne 1947–1997, compared with Australian national twinning incidence

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The incidence of dizygotic (Dz) twinning can be used as an index of natural human fertility. A retrospective study was done at The Royal Women's Hospital, Australia, to see whether the dizygotic to monozygotic (Mz) twinning ratio from one hospital can accurately reflect the national incidence of Dz twinning. The yearly twinning incidence from 1947–1997 was expressed as a Dz:Mz ratio, standardised for maternal age and plotted against previously published national statistics. The proportion of mothers born in Asia (of both singleton and multiples) between 1983–1997 was analysed to see whether different racial mixes might influence twinning trends. There were 5275 twins born of known sex and maternal age between 1947–1997. The age-standardised Dz:Mz ratio increased non-significantly from 1.39 in 1947 to 2.29 in 1953 ($P = 0.08$), underwent a significant decline to 0.73 in 1977, then remained stable until 1997 ($P > 0.05$). The same trends were also apparent when the data was pooled into 2-year groups with the increase from 1947/48–1953/54 becoming highly significant ($P < 0.009$). These trends observed in the hospital-based data were in close agreement with those found in the national statistics, with the exception of a rise in 1977–1982 only reflected in the Australia-wide data. In 1993, 2.6% of mothers were born in Asian countries; by 1997, this had risen to 10.6%. We found that the Dz:Mz ratio from one hospital closely reflects national twinning trends. Prospective studies must account for race, and would need around 200–300 twin pairs per year to minimise fluctuations of the ratio. Twin Research (2000) 3, 12–16.

Keywords: fertility rates, twins, trends

Introduction

There has been much recent debate over whether human fertility is on the decline.[1] It is therefore vitally important that there should be global monitoring of natural human fertility. The incidence of spontaneous Dz twinning in a population provides a useful index of male plus female fertility since it provides an indication of the ovulation rate, fertilisation rate (which could be affected by any decline in sperm counts), implantation rate, or embryonic and foetal survival rate.[2–4]

Beginning in the 1960s there was a uniform worldwide decline in Dz twinning rates in every developed country where the incidence was recorded.[3,4] The exact cause of the fall is unknown, although it may have been the consequence of post oral contraceptive pill infertility.[4] A subsequent global upturn in Dz twinning began in the mid 1970s[4] and is almost certainly caused by increasing use of ovulation-inducing agents such as clomiphene citrate and gonadotrophins, which substantially increases the incidence of Dz twinning.[5,6] The iatrogenic twinning has meant that the raw incidence of Dz twinning taken from national statistics no longer reflects spontaneous twinning rates and natural fertility.

We have previously proposed that to monitor fertility, prospective hospital based data be collected to exclude all twins arising from ovulation-inducing agents. To overcome bias due to the selective referral to hospitals of mothers carrying twins, the data could be expressed as a Dz:Mz ratio.[4]

The purpose of this study was to see if the ratio derived from one hospital accurately reflects the Dz twinning trends of the population. Therefore data was collected on the number and sex of all twins born in The Royal Women's Hospital in Melbourne, Australia, from 1947 to 1997, and compared with previously published Australian national statistics on twinning.[7] The Royal Women's is a public tertiary teaching hospital, one of only two women's hospital in Melbourne.

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Methods

The date of birth, maternal age and sex of all twins born at The Royal Women's Hospital, Australia, between 1947 to 1997 was obtained from hospital records. A small number of twin births where this information was not complete were excluded. An estimate of the total number of Dz twins was made by doubling the number of opposite-sexed twin pairs. (This calculation assumes that there are equal numbers of opposite and same-sexed dizygotic twin pairs.) The remainder were assumed to be Mz. This is known as Weinberg's differential method.[8]

The data was then expressed as an annual Dz:Mz ratio. The important influence of maternal age was corrected for by indirect standardisation, using the method described by Fellman and Erikson,[9] with the slight modification of first converting all data to a Dz:Mz ratio. The reference population was taken from the published national Australian statistics for the year 1955.[7] The purpose of standardisation is to counteract the effect of maternal age by adjusting the annual ratio/rate down if there were predominantly older mothers in that year, or increasing the ratio if there were mostly younger mothers.

The data were graphed against the national age-standardised twinning rates previously published by Doherty and Lancaster.[7] The national twinning rates, also standardised against the year 1955, increased from the late 1800s until 1953, declined until 1977, then increased until 1982 (the last year for which the national statistics are available). The χ^2 test for trend was performed to see whether the hospital data mirrored these trends. In order validly to apply χ^2, the relative number of Dz and Mz twin pairs were estimated from the age-standardised ratio and total number of twins for that year, then rounded to the nearest whole number.

The data was then smoothed by pooling the twin pairs into two-yearly groups. (The raw biannual Dz:Mz ratio was first determined, then standardised for maternal age.) Assuming that Mz twinning is constant at about 4/1000 maternities,[4] an estimate of the Dz per 1000 maternities could be made by quadrupling the ratio. This was plotted against the average of each consecutive 2-year group in the age-specific national twinning rates published by Doherty and Lancaster.[7] Trends were again analysed using the χ^2 test for trend.

Since Doherty and Lancaster[7] did not distinguish between iatrogenic and spontaneous twinning, the same was done in this study so that the two datasets could be validly compared. This means that from the late 1960s onwards, when ovulation induction agents were in widespread use, both datasets no longer reflect trends in human fertility.

The annual proportion of mothers born in Asian countries giving birth to singletons or twins from 1983 to 1997 was recorded to see whether different racial mixes might influence twinning trends. A graph was prepared to show how the number of twin pairs affected the standard error of the mean estimate of the Dz:Mz ratio.

Results

Between 1947 to 1997, there were 5275 twin pairs of known sex born to women of known age at The Royal Women's Hospital. The mean number collected per year was 106 twin pairs, with a range of 36 to 160.

Figure 1 shows the standardised Dz:Mz ratio, with the number of twin pairs per year, plotted against the previously published Australian national Dz twinning rates.[7] There was an increasing trend from 1.39 in 1947 to 2.29 in 1953 which did not reach statistical significance ($P = 0.08$), a highly significant decline to 0.73 in 1977 ($P < 0.001$), after which the ratio remained stable until 1997 ($P > 0.05$).

When the data was grouped into 2-year pools, the increase in the Dz:Mz ratio from 1.64 in 1947/1948 to 3.22 in 1953/54 became highly significant ($P < 0.009$), as was a subsequent decline to 1.03 in 1977/78 ($P < 0.001$). A stable rate persisted until 1995/96 ($P > 0.05$). Therefore, with the exception of a short rise in 1977–1982 only reflected in the Australian-wide data,[7] the trends observed in the hospital-based data were in close agreement with those found in the national statistics.

The estimated Dz incidence, made by quadrupling the bi-yearly ratio, is shown in Figure 2. The trends fluctuate considerably less than in Figure 1. This is especially true of the last decade where there were between 260 to 313 twin pairs at each point.

Figure 3 shows that in 1993, 2.6% of mothers were born in Asian countries; by 1997 this had risen to 10.6%.

Figure 4 shows that the relationship between the number of twin pairs collected per year and the standard error follow an exponential relationship. Considerable decreases in the standard error can be achieved if 200 twin pairs were collected; any further increases only minimally reduce the standard error.

Discussion

This study has shown that data collected from one hospital and expressed as a Dz:Mz ratio closely reflect the incidence of dizygotic twinning observed nationally over a 40-year period. It confirms that the

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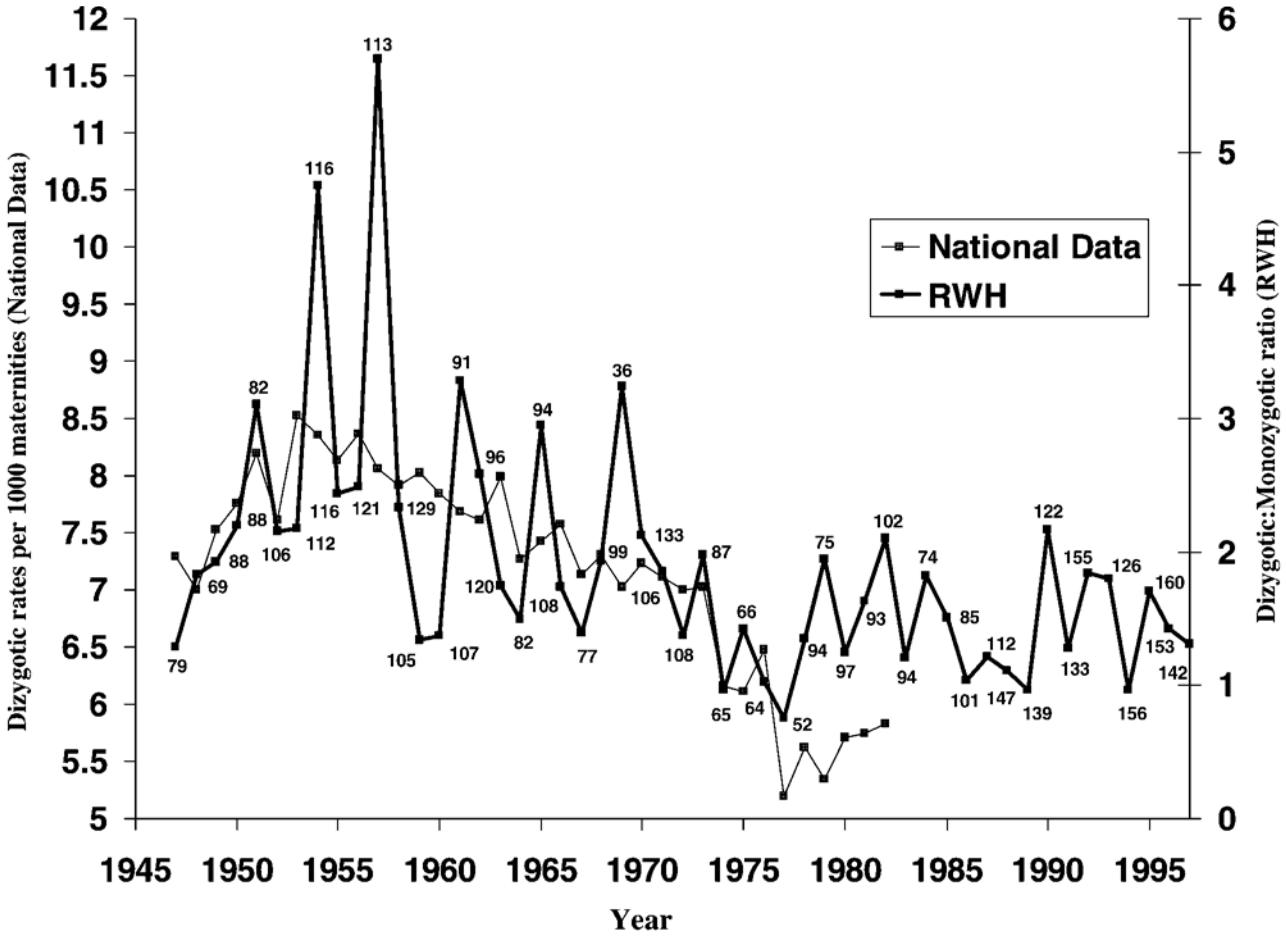

Figure 1 Standardised annual twinning rates: Royal Women's Hospital (dizygotic to monozygotic ratio), 1947–1997; and National dizygotic twinning incidence (dizygotic twins per 1000 maternities), 1947–1982, published by Doherty and Lancaster (1986). Number of twin pairs per year given on the curve

Dz:Mz ratio is an accurate method for measuring fertility prospectively.

This is the first report of twinning rates which has not shown a persistent increase in twinning throughout the 1980s and 90s. All other developed countries have found a continuous rise since the 1970s, most likely caused by the increasing use of ovulation-inducing agents. This iatrogenic twinning means that published national twinning trends from the 1970s onwards no longer reflect natural human fertility. Countries reporting the rise include Denmark,[10] The Netherlands,[11] Italy,[12] England and Wales,[13] Scotland,[14] Luxembourg,[15] USA,[16] Israel[17] and Hong Kong.[18] Such a continuing rise would also have been expected in The Royal Women's Hospital. In the national statistics[7] there is a rise in the years 1977–1982 which is likely to have continued. The most likely explanation is that the expected increase was offset by an increasing proportion of Oriental patients delivering at The Royal Women's Hospital, since their Dz twinning rate is half that of Caucasians.[19] There has been a substantial growth of the Asian population in the suburbs around The Royal Women's Hospital over the past two decades. This is reflected in Figure 3 which shows that the proportion of all mothers who were born in Asian countries (both singleton and multiple births) has increased from 2.6% to 10.6% in the last 15 years. It must also be remembered that 10.6% is a very conservative estimate since it would not include second generation Asians, nor those of Oriental descent migrating from non-Asian countries.

This provides an important lesson for those using the Dz:Mz ratio; race must also be accounted for as well as maternal age. This is especially relevant in countries such as Australia where racial demographics are undergoing rapid change. The only practical way to correct for race is by splitting the data into three racial groups before applying the ratio; Caucasians (whose dizygotic twinning incidence is at around 8/1000 maternities), Orientals (4/1000 maternities) and Negroids (10–40/1000 maternities).[19] The

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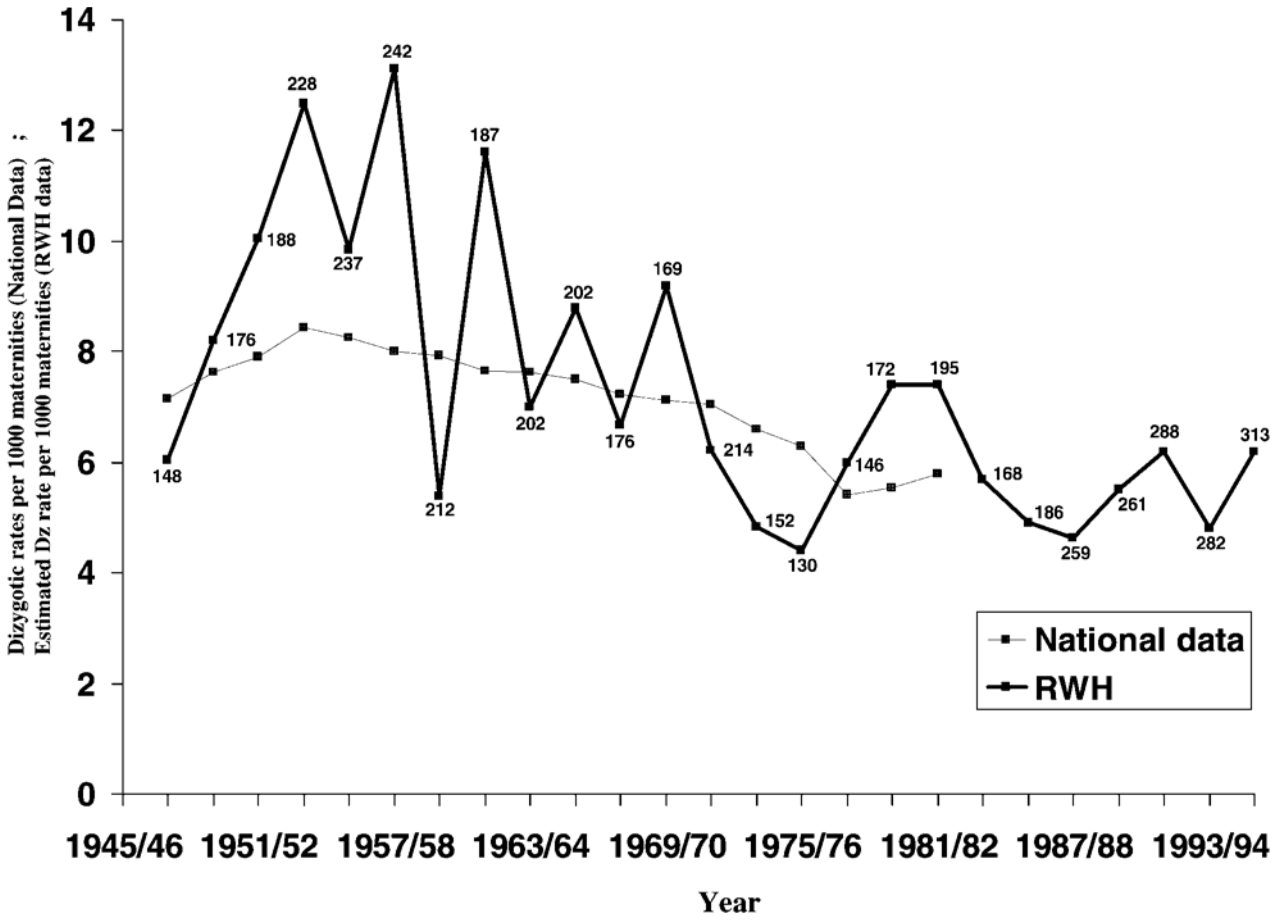

Figure 2 Standardised twinning rates pooled into 2-year groups: Royal Women's Hospital ('estimated' dizygotic twinning per 1000 maternities) 1947/48–1995/1996; and National dizygotic twinning incidence (dizygotic twins per 1000 maternities), 1947/48–1981/82, modified from data published by Doherty and Lancaster.[7] Number of twin pairs per year given on the curve

number of twin pairs in minority groups may be too small to calculate the Dz:Mz ratio with any precision.

The results of this study have shown that fluctuations could be minimised substantially when numbers were pooled into 2-year bands. The rise predicted by the national data in 1947–1953 just failed to reach significance when the annual ratio was analysed but became highly significant when the data was pooled (Figure 2 vs Figure 3). Furthermore, the curve was particularly smooth over the last decade (1987/88 to 1995/96) when there were over 260 twin pairs at each point. Figure 4 shows that if 200 or more twin pairs are collected, the standard error becomes very small; any further increase in numbers only minimally affects the error. However, even greater numbers would still further minimise fluctuations. Those using the Dz:Mz ratio prospectively should therefore aim to collect at least 200–300 spontaneous twin births per year. This would probably require a multi-centre approach.

Figure 2 also clearly shows that provided there is a sufficiently large sample, the Dz:Mz ratio could be used to derive the twinning rate per thousand maternities. The value of calculating such an estimate is that it would enable comparisons to be made with previously published data. However, yet another estimate theoretically introduces more errors, and therefore it should always be expressed as an 'estimated' Dz twinning rate per thousand maternities.

This study has shown that the Dz:Mz ratio is an accurate method of monitoring changes in the incidence of Dz twinning. It can therefore now be used to answer some important longstanding questions. Retrospective data from Africa may shed light as to the cause of the uniform fall in Dz twinning in the developed world throughout the 1960s. Studies among migrant Asian populations could help determine whether the low incidence of Dz twinning is genetically or environmentally determined. Prospective studies could be implemented globally as a

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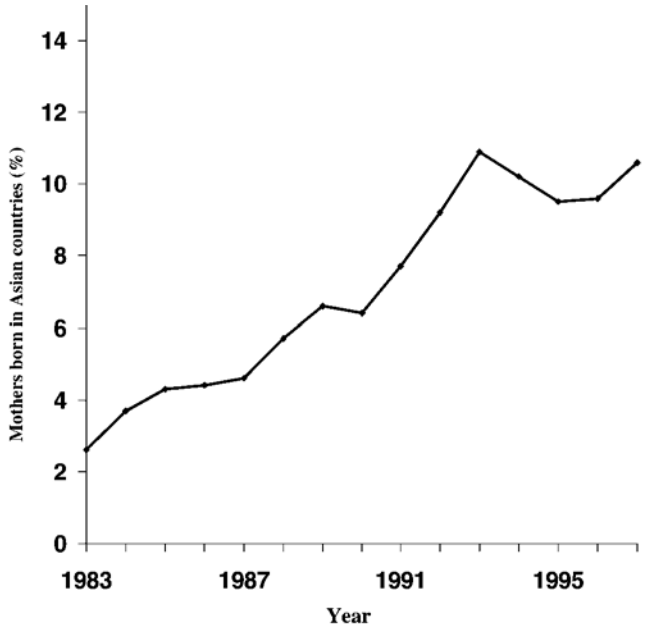

Figure 3 Proportion of mothers at Royal Women's Hospital born in Asian countries (both singleton and multiple pregnancies)

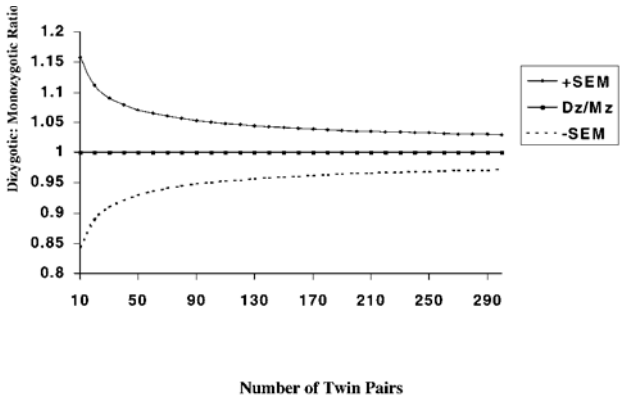

Figure 4 Standard error of the mean (SEM) estimate of the dizygotic to monozygotic ratio has been arbitrarily chosen as 1

cheap and accurate method to monitor changes in natural human fertility over time.

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