

A Multiple Pregnancy Register in the North of England

Svetlana V. Glinianaia¹, Judith Rankin¹, Chris Wright², Stephen N. Sturgiss³, and Marjorie Renwick²
on behalf of the Northern Region Perinatal Mortality Survey Steering Group

¹Department of Epidemiology & Public Health, The Medical School, University of Newcastle, Newcastle upon Tyne, UK

²Northern Region Perinatal Mortality Survey, Regional Maternity Survey Office, 25 Claremont Place, Newcastle upon Tyne, UK

³Fetal Medicine Unit, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne, UK

A regional population-based Multiple Pregnancy Register was established in 1998, with the aim of collecting detailed information on multiple pregnancies to enable research into mortality and morbidity in multiples. Multiple pregnancies are notified to the Register as soon as they are detected, irrespective of whether they resulted in a spontaneous abortion, termination of pregnancy or registered birth. Nine hundred and twenty-six twin pregnancies were recorded during 1998–99, giving a twinning rate of 14.8 per 1000 maternities (rate at birth 13.0 per 1000 maternities). Sixty one per cent of twin pregnancies were detected before 13 weeks of gestation. Chorionicity was determined in 82.6% of 849 twin maternities with at least one stillbirth or livebirth. The fetal loss rate before 24 weeks of gestation was 10.5% (194/1852). The perinatal and infant mortality rates were 40.6 per 1000 births and 32.6 per 1000 livebirths respectively. A prospective Multiple Pregnancy Register not only allows monitoring of trends in multiple birth rates and mortality, but also etiological research and long-term follow-up studies.

The continued increase in multiple birth rates over the past decade (Derom, 1995; Imaizumi, 1998; Kiely & Kiely, 2001; Loos et al., 1998) has raised concern about their rising contribution to fetal and infant mortality and to childhood disability (Bergh et al., 1999; Blickstein & Weissman, 1999). The twinning rate in the Northern Region of England has also been increasing, with the perinatal mortality rate in twins 5.5 times that in singletons (Glinianaia et al., 1998). Building on the excellent clinical network already in place in the Northern Region, a regional population-based Multiple Pregnancy Register (MPR) was established in January 1998. The remit of this prospective survey of multiple pregnancies was to determine: multiple birth rates, rates of fetal and infant losses, frequency of disorders of intrauterine development, frequency of obstetric complications, correlation of outcomes with chorionicity and zygosity, long-term outcomes and contributions to obstetric and neonatal workloads. This register records a multiple pregnancy from the first trimester ultrasound screening, where available, irrespective of whether the pregnancy resulted in a spontaneous abortion, termination of pregnancy or registered birth.

Materials and Methods

Population

The former Northern Region (now part of the Northern & Yorkshire Region) was one of the 14 administrative regions

into which the National Health Service in England and Wales was divided before its reorganization in 1994. The region is a well defined geographical area comprising five counties (Tyne and Wear, Cleveland, Cumbria, Durham, and Northumberland) with a mixed urban/rural population of nearly 3 million and approximately 32,000 deliveries per year. The population of the Northern Region is relatively stable making follow-up studies more manageable (Wariyar & Richmond, 1989).

The Regional MPR was established on 1 January 1998 at the Regional Maternity Survey Office (RMSO) which houses several ongoing regional registers, including the Northern Perinatal Mortality Survey (PMS) (Northern Regional Health Authority Coordinating Group, 1984) and the Northern Congenital Abnormality Survey (NorCAS) (Northern Regional Survey Steering Group, 1992). The Northern Region has an excellent network of interested and motivated clinicians who have been involved in providing data for the PMS since 1981 and the NorCAS since 1984. In 1997, the Clinical Director of the RMSO wrote to all regional consultant obstetricians, pediatricians, ultrasonographers and pathologists informing them of the proposal to establish a MPR from the 1 January, 1998, and the reasoning behind it. An information poster, pre-paid notification cards and obstetric notes stickers were attached to the covering letter. The regional clinicians have strongly welcomed and supported this initiative.

The MPR was established with the remit of collecting data on all multiple pregnancies arising within the Northern Region whether resulting in a spontaneous abortion, termination of pregnancy or registered birth (live and stillbirths). All multiple pregnancies are notified to the RMSO as soon as they are detected, either antenatally or perinatally. A notification card with basic mother's details (name, address, date of birth, place of delivery, hospital record number), information on multiple pregnancy diagnosed (twins, triplets or other; if antenatal diagnosis: estimated gestation at diagnosis,

Address for correspondence: Dr. Svetlana V. Glinianaia, Department of Epidemiology and Public Health, School of Health Sciences, The Medical School, University of Newcastle, Framlington Place, Newcastle upon Tyne, NE2 4HH, United Kingdom. Email: Svetlana.Glinianaia@ncl.ac.uk

estimated date of delivery, chorionicity, date of diagnosis; if postnatal diagnosis: estimated gestation at delivery, date of delivery; current status: pregnancy continuing or pregnancy outcome), date of notification and name of person notifying. After delivery, all maternity units complete a two-page form with more extended information on the mother's details, pregnancy, chorionicity and the outcome. All maternal units are reminded to send the placentas for pathological examination, and pathologists have been requested to determine chorionicity when examining the placentas. Data from the notification card and the form are entered onto a database, checked for duplication and cross validated with the PMS, NorCAS and Northern Diabetic Pregnancy Survey databases. Annual cross validation with the Office for National Statistics (ONS) has demonstrated superior case ascertainment. Feedback to the clinicians is provided in the form of an annual RMSO study day, annual report and by personal communication of the RMSO staff to individual maternity units.

The total number of births in the Northern Region for 1998–1999 was obtained from the ONS. All data are based on the date of birth.

Definitions

The *twinning rate at birth* is the number of twin maternities resulting in births of both twins, either livebirth or stillbirth¹, per 1000 maternities at birth. The number of maternities at birth is calculated as the number of all registered singleton births (equals the number of singleton maternities at birth) plus the number of registered multiple maternities at birth (i.e., a half of twin births, a third of triplet births etc.). The *twinning rate* is defined as the number of twin maternities with at least one livebirth or stillbirth, including maternities where there has been an early or late fetal loss per 1000 maternities with at least one stillbirth or livebirth. The *total twinning rate* is calculated as the number of all detected twin pregnancies regardless of the outcome of pregnancy (spontaneous abortion, termination of pregnancy or registered birth) or gestational age per 1000 detected pregnancies (includes singleton and multiple maternities at birth plus extra twin maternities detected antenatally regardless of the outcome).

Ethical Approval

The Regional Multi-Centre Research Ethics Committee gave approval for data collection.

Statistical Analysis

Analysis was carried out using the Statistical Package for the Social Sciences (SPSS for Windows) (Norusis, 1993). Chi-square tests were used to test differences in proportions. Statistical significance was accepted at the $p < .05$ level.

Results

Table 1 shows some vital statistics as proposed at the 10th International Congress on Twin Studies for the comparison of basic perinatal data between different countries or regions (Derom et al., 2001).

Table 2 shows gestational age at diagnosis of twin pregnancies by routine ultrasound. Nearly 61% of twin

Table 1

Vital Statistics in the Northern Region in 1998–99 Following the Protocol Proposed by Derom et al. (2001) at the 10th International Congress on Twin Studies

| Country or region | 1998–99 Vital Statistics | |
|---|----------------------------|---------------|
| | Northern Region of England | |
| Inhabitants | 3 million | |
| Year of birth | 1998 | 1999 |
| Births | | |
| Singletons | 31332 | 30271 |
| Twins | 836 | 782 |
| Triplets | 33 | 39 |
| Origin of (provider of) the data | ONS, MPR | ONS, MPR |
| Prevalence of twin maternities | 13.2 per 1000 | 12.7 per 1000 |
| Same-sex pairs | 276 | 253 |
| Opposite-sex pairs | 141 | 133 |
| MZ/DZ proportions according to Weinberg's rule | 32.4% / 67.6% | 30.6% / 69.4% |
| Fetal and early neonatal deaths (perinatal mortality rate per 1000) | 24 (28.7) | 42 (53.7) |

Note: the number of same-sex and opposite-sex pairs are not equal to the total number of twin pairs due to the stillbirths with indeterminate sex (one for 1998 and five for 1999)

ONS = Office for National Statistics

MPR = Multiple Pregnancy Register

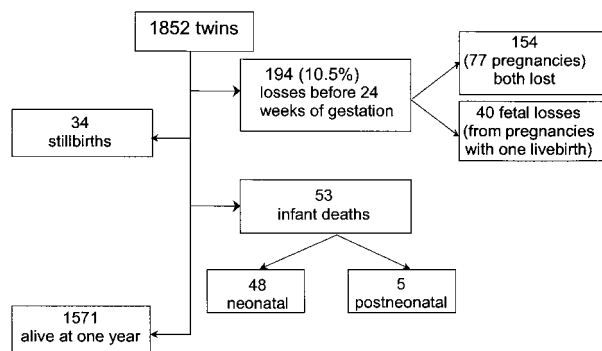
Table 2

Gestational Age at Diagnosis of a Twin Pregnancy (in Completed Weeks)

| Gestation at diagnosis (weeks) | Number | % |
|--------------------------------|--------|------|
| < 9 | 201 | 21.7 |
| 9–12 | 363 | 39.2 |
| 13–18 | 260 | 28.1 |
| 19–24 | 73 | 7.9 |
| > 24 | 11 | 1.2 |
| Not recorded | 18 | 1.9 |
| Total | 926 | 100 |

pregnancies were diagnosed before 13 weeks of gestation and a further 28% were detected by 18 weeks.

Overall, there were 62,441 total maternities in the Northern Region (ONS data) in 1998–1999 and 809 twin maternities at birth, giving a twinning rate at birth of 13.0 per 1000 maternities. The twinning rate is higher when the maternities with at least one livebirth or stillbirth (849) are included (13.6 per 1000) and much higher when all twin pregnancies notified to the MPR (926) are included (14.8 per 1000 maternities). Chorionicity was determined in

**Figure 1**

Outcome of twin pregnancies, Northern Region 1998–99.

82.6% of 849 twin maternities with at least one stillbirth or livebirth.

Figure 1 presents the outcome of all registered twin pregnancies. One-thousand, eight-hundred and fifty-two twins were notified: 194 of them were lost before 24 weeks of gestation giving a recognised fetal loss rate of 10.5%, and there were 1658 twin births, including 40 liveborn twins from twin pregnancies with one fetal loss before 24 weeks of gestation and a livebirth. Of 194 fetal losses, in 77 twin pregnancies both twins were lost as a result of a spontaneous abortion (48) or a termination of pregnancy (29); further 40 twin pregnancies resulted in a livebirth and an early or late fetal loss (24 before 13 weeks of gestation including “vanishing” twins). Of 1658 twin births, there were 34 stillbirths (31 antepartum and 3 intrapartum) and 53 infant deaths (35 early neonatal, 13 late neonatal and 5 postneonatal); 1571 twins were alive at one year. The perinatal and infant mortality rates were 40.6 per 1000 births and 32.6 per 1000 livebirths respectively.

Discussion

The twinning rate in the Northern Region has been increasing consistently since 1990 (Glinianaia et al., 1998), and continues to rise. The increase in multiple pregnancy rates is an important public health issue. The proportion of multiple births with birthweight below 1500g is dramatically higher than in singletons. As these babies are known to be at high risk of perinatal mortality and morbidity, they represent a high cost in terms of an increased patient load to neonatal intensive care units and an increase in long-term morbidity and disability.

A prospective population-based MPR was established in the Northern Region from January 1998 with the remit of extending information on multiple pregnancies and enabling research into the high mortality and morbidity in multiples. One of the advantages of the Northern MPR is that multiple pregnancies are notified from the first trimester ultrasound screening where available (61% were diagnosed before 13 weeks of gestation in 1998–99), irrespective of whether the pregnancy resulted in a spontaneous abortion, termination of pregnancy or registered birth. The East Flanders population-based Prospective Twin Survey is the only European register containing full

perinatal data including information on placentation (Loos et al. 1998). However, twins are ascertained at birth in this register; early fetal losses detected by ultrasound are not included. Thus, the Northern MPR is unique within the UK and in Europe, in that the surveillance of twin pregnancies begins in the first trimester.

The MPR has several advantages over the national birth registration system. Multiple birth registrations by the ONS are incomplete because of the legal definition of what is registrable. A number of twin pregnancies may be registered as singletons with the ONS, due to the very early loss of one fetus. An early twin death diagnosed by ultrasound is likely not to be registered. Also, despite the legal requirement to register a fetus papyraceus, this does not always occur (Pharoah & Cooke, 1997). As a consequence, the regional twinning rate based on the ONS data (the twinning rate at birth) is lower and less accurate than the twinning rate based on the MPR data, as the former misses twin maternities resulting in a livebirth and a fetal loss before 24 weeks of gestation.

A further advantage is the collection of additional information by the regional MPR. This information is extremely important for analyzing perinatal mortality causes, etiological research and long-term follow-up studies; for example, accurate gestational age and chorionicity (chorionicity was determined in 82.6% of twin maternities with at least one stillbirth or livebirth). It is recognised now that chorionicity has a greater effect on the perinatal outcome of twins than zygosity. It has been shown that monochorionic twins have a significantly higher perinatal mortality than dizygotic (always dichorionic) twins whereas perinatal mortality in monozygotic dichorionic and dizygotic twins was comparable (Loos et al., 1998).

Recording the sex of a fetal death, especially if it was a fetus papyraceus, in the MPR is also likely to be more accurate than in the national statistics, because it is based on the information derived from the hospital notes and the post-mortem. It has also been reported that if the sex of a fetus papyraceus was indeterminate, it was always coded as male in the national statistics (Pharoah, 1999).

The MPR is linked with other ongoing regional registers, which are also housed at the RMSO, the PMS, NorCAS and Diabetic Pregnancy Survey, and also with the regional Fetal Medicine Unit, which holds its own database. These valuable links enable regular cross-validation, thereby enhancing case ascertainment as well as quality, completeness and accuracy of the data.

The Northern Region has an excellent clinical network which has strongly welcomed and supported the MPR. A network of interested and motivated clinicians is an important prerequisite for establishing and maintaining the successful functioning of a MPR.

The MPR provides an opportunity to develop population-based research on a particularly vulnerable subgroup of pregnancies. This might include studies of the management and outcome of multiple pregnancy, and investigations of service provision and quality of care issues. The availability of data on all pregnancies, and not just those with adverse outcomes, enables detailed analysis of the factors associated

with poor outcome and a more appropriate interpretation of explanations for variations in outcome.

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Footnote

- 1 *Early fetal loss* is defined as any identifiable fetal loss before the end of the thirteenth week of gestation (including vanishing twins). *Late fetal loss* is defined as any identifiable fetal loss after thirteen completed weeks and before the end of the 24th week of pregnancy. *Spontaneous abortions* combine early and late fetal losses. *Termination of pregnancy* is a legal induced abortion due to congenital malformations or other medical reasons undertaken before the end of the 24th week of pregnancy (if later defined as stillbirth). *Stillbirth* is defined as fetal death occurring at any gestation but delivered after 24 completed weeks of gestation. *Early neonatal death* is the death, following livebirth, of a baby before completing seven days of life. *Perinatal deaths* combine stillbirths and early neonatal deaths. *Late neonatal death* is the death of an infant on or between the 8th and 28th day of life. *Neonatal deaths* combine early and late neonatal deaths. *Post neonatal death* is the death of an infant on or between the 29th and the 365th day of life. *Infant death* is the death, following livebirth, of an infant before completing 365 days of life. *Perinatal mortality rate* is calculated per 1000 registered twin births. *Infant mortality rate* is calculated per 1000 twin livebirths.

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