Public Health Aspects of Preterm Birth
Studies using Scandinavian population-based data

Akademisk avhandling

som för avläggning av medicine doktorsexamen
vid Sahlgrenska Akademin vid Göteborgs Universitet
kommer at offentligen försvaras i kvinnoklinikens aula,
Sahlgrenska Universitetssjukhuset/Östra
torsdagen den 5 juni 2008 klockan 13.00

av

Nils-Halvdan Morken
Legitimerad läkare

Fakultetsopponent:
Professor Jason Gardosi
West Midlands Perinatal Institute, Birmingham, Storbritannien

Avhandlingen baseras på följande arbeten:

I. Morken NH, Källén K, Hagberg H and Jacobsson B, Preterm birth in Sweden 1973-2001: rate, subgroups and effect of changing patterns in multiple births, maternal age and smoking. Acta Obstet Gynecol Scand 2005; 84: 558-65.

II. Morken NH, Källén K and Jacobsson B, Fetal growth and onset of delivery: a nationwide population-based study of preterm infants. Am J Obstet Gynecol 2006; 195: 154-61.

III. Morken NH, Vogel I, Källén K, Skjærven R, Langhoff –Roos J, Kesmodel U, Jacobsson B, Reference population for international comparisons and time trend surveillance of preterm delivery proportions in three countries. Manuscript.

IV. Morken NH, Källén K and Jacobsson B, Outcomes of preterm children according to type of delivery onset: a nationwide population-based study. Paediatric and Perinatal Epidemiology 2007; 21: 458-64.

V. Morken NH, Källén K and Jacobsson B, Prediction of spontaneous preterm delivery by combining logistic and Bayesian methods. Manuscript.

Handledare: Doc. Bo Jacobsson   Bihandledare: Doc. Karin Källén
Institutionen för kliniska vetenskaper   Tornblad Institutet
Sahlgrenska akademiet   Lunds Universitet
Göteborgs Universitet

Avhandlingen kommer at försvaras på engelska

ABSTRACT

Morken Nils-Halvdan. 2008. **PUBLIC HEALTH ASPECTS OF PRETERM BIRTH Studies using Scandinavian population-based data**. Institute of Clinical Sciences, Department of Obstetrics and Gynecology at Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

Background: Preterm birth is an unresolved serious global health problem, research on which must be multi-disciplinary, with assessment of risk factors and causative agents at many levels of observation, such as the public health level. The general aim of this thesis was to describe, assess and explore public health aspects of preterm birth.

Material and Methods: Scandinavian population-based data from the three Medical Birth Registers in Sweden, Denmark and Norway and the Swedish Hospital Discharge Register were used. Preterm birth in Sweden during the Birth Register era from 1973 to 2001 was studied and subgroups of preterm birth during 1991-2001 were assessed. The association between spontaneous preterm birth and fetal birth weight deviating from the population mean was explored. We propose the use of reference populations as a supplement in international comparison of baseline differences in preterm birth proportions and for time trend surveillance. The respective outcomes in spontaneous and iatrogenic preterm-born infants were examined and compared. Models for prediction of spontaneous preterm birth at <34 and <37 weeks were developed and validated in a test population by combining logistic regression and Bayesian methods.

Results: **(I)** The proportion of preterm birth (<37 weeks) in Sweden decreased from 6.3% in 1984 to 5.6% in 2001 (p<0.0001), a decrease evident among singleton births at 34-36 gestational weeks. The composition of preterm subgroups was similar to that found in populations with higher preterm birth rates. **(II)** Associations between smaller than the population mean and spontaneous preterm birth were evident in all gestational age groups. The largest risk was found at 28-31 gestational weeks and birth weight <-3SD (OR: 13.3; 95% CI: 10.3-17.2). Spontaneous preterm infants born at 34-36 gestational weeks more often weighed 1-1.9 SD (OR: 1.1; 95% CI: 1.1-1.2) or 2-2.9 SD (OR: 1.6; 95% CI: 1.5-1.7) above the expected mean. **(III)** The national preterm delivery rate (<37 weeks) increased from 5.3% to 6.1% (p<0.001) in Denmark and from 6.0% to 6.4% (p=0.006) in Norway, but remained unchanged in Sweden, during 1995-2004. In Denmark, the preterm delivery rate in the reference population increased significantly (5.3% to 6.3%, p<0.001), as did the spontaneous preterm delivery rate in the reference population (4.4% to 6.8%, p<0.001). No similar increase was evident in Norway. In Sweden, rates in the reference population remained stable. **(IV)** Spontaneous preterm infants were at increased risk of cerebral palsy at gestational age 28-31 weeks (HR: 1.86; 95% CI: 1.12-3.10) and of sepsis at gestational age 32-33 weeks (HR: 1.58; 95% CI: 1.28-1.96). Other outcome variables were associated with iatrogenic preterm birth, particularly respiratory and gastrointestinal diagnoses. **(V)** Six prediction models were developed. The area under the receiver operator curve in the test population ranged from 0.77 (95% CI: 0.76-0.77) to 0.59 (95% CI: 0.57-0.61) for spontaneous preterm birth at <37 weeks and from 0.80 (95% CI: 0.79-0.81) to 0.64 (95% CI: 0.62-0.67) for spontaneous preterm birth at <34 weeks. For each delivery in the test population, the model that utilized the available information to the greatest extent was used, and total areas under the receiver operator curve for spontaneous preterm birth at <34 weeks (0.74, 95% CI: 0.73-0.75) and <37 weeks (0.71, 95% CI: 0.7-0.71) were calculated.

Conclusions: The proportion of preterm birth in Sweden has decreased since the mid-eighties. Deviation of fetal birth weight from the expected mean is associated with spontaneous preterm delivery. Reference populations may prove to be a valuable supplement in assessments of national preterm delivery proportions in connection with public health surveillance. Spontaneous preterm birth and iatrogenic preterm birth are associated with different pediatric outcomes. Spontaneous preterm birth can be predicted by using the proposed models, which might be applicable in clinical assessment of risk.

Link to thesis: http://hdl.handle.net/2077/10125