

The validity of the diabetes mellitus diagnosis in the Medical Birth Registry of Norway

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ABSTRACT

The Medical Birth Registry of Norway (MBRN) has registered all births in Norway since 1967 and diabetes is registered as a maternal diagnosis. We present original data assessing the validity of the diabetes diagnosis. Among women with known pre-gestational type 1 diabetes, 97% of births during 1976-1998 (old registration form) were identified as pre-gestational diabetes in the MBRN. For births 1999-2004 (new registration form), 94% were identified as pre-gestational diabetes in the MBRN. Of cases coded as pre-gestational diabetes by the MBRN, 80% were confirmed by the medical record for births during 1998, while more than half of the births incorrectly coded as pre-gestational diabetes really were gestational diabetes. Among births coded as gestational diabetes, 89% were confirmed in the medical record. In conclusion, the sensitivity of the pre-gestational diabetes diagnosis in the Medical Birth Registry of Norway was very good, particularly in the earlier period, but the information in the MBRN on births before 1999 was not sufficient to classify pre-gestational diabetes as type 1 – or type 2 diabetes. The type of diabetes can be specified for births from 1999 onwards, but the predictive values are unknown. The predictive value for pre-gestational diabetes in 1998 was less than optimal but acceptable for a routine registry not specialised for diabetes.

NORSK SAMMENDRAG

Gravide kvinner med type 1 diabetes har økt risiko for komplikasjoner i svangerskapet, medfødte misdannelser og dødfødsel. Data fra medisinsk fødselsregister (MFR) har vært grunnlag for viktige publikasjoner om risiko for komplikasjoner hos gravide kvinner med diabetes. I tillegg til å gi en kort oversikt over disse publikasjonene presenterer vi data om validiteten til diabetesdiagnosen. Av fødsler til og med 1998 med kjent type 1 diabetes før svangerskapet basert på opplysninger fra Norsk diabetesregister (NDR) ble 97% registrert som diabetes før svangerskapet i MFR (gammelt registrerings skjema). For fødsler 1999-2004, ble 94% kodet som pre-gestasjonell (type 1- eller type 2-) diabetes. Ved sammenligning med sykehusjournalen til kvinner identifisert i MFR med diabetesdiagnose før svangerskapet (fødsler i 1998) ble diabetes før svangerskapet i følge MFR bekreftet i journalen i 80% av tilfellene. Av fødsler kodet med svangerskapsdiabetes ble 89% bekreftet i journalen. Vi konkluderer med at sensitiviteten for pre-gestasjonell diabetes er meget god, spesielt for fødsler før 1999, men MFR kan for denne perioden ikke brukes til å klassifisere pre-gestasjonell diabetes hos mor som type 1- eller type 2 diabetes. For fødsler fra og med 1999 kan type diabetes spesifiseres, men prediktiv verdi for disse diagnosene er ikke undersøkt. Prediktiv verdi for diagnosen pre-gestasjonell diabetes i MFR for fødsler i 1998 er ikke optimal, men akseptabel for et rutine register som ikke har diabetes som hovedfokus.

INTRODUCTION

Diabetes is a heterogeneous group of diseases defined by hyperglycaemia, caused by impaired insulin secre-

tion, insulin action, or both. In addition to rare monogenic and syndromic forms, the main types are type 1, characterised by destruction of the insulin producing beta-cells in the pancreatic islets of Langerhans and

complete dependency of insulin injections, and type 2 diabetes, characterised by a combination of insulin resistance and impaired secretion (1,2). Gestational diabetes is defined as diabetes or impaired glucose tolerance recognized for the first time during pregnancy, regardless of actual time of onset and insulin dependency or treatment (1). Details of diagnostic criteria have changed over time and are beyond the scope of this paper, but interested readers are referred to the publications from the World Health Organization and the American Diabetes Association (1-4). Norwegian guidelines for diagnosis and treatment of diabetes, essentially based on the international ones, are given by The Norwegian College of General Practitioners (2005) (<http://www.nsamdiabetes.no/>) and by the Norwegian Society of Gynaecology and Obstetrics (2006) (<http://www.legeforeningen.no/index.gan?id=40692&subid=0>). Gestational diabetes is a heterogeneous group of conditions. The diagnostic criteria are complex and debated, and there is no systematic study of the actual clinical practice regarding screening, "case-finding" or diagnostic criteria in Norway. Ideally, women with gestational diabetes should be reclassified after pregnancy (1), but this information is not available in the Medical Birth Registry of Norway.

Diabetes has long been recognized as a serious condition in pregnant women, with excess risk for a number of complications for mother and foetus, such as stillbirth, postnatal mortality, congenital malformations, macrosomia, preterm birth, and pre-eclampsia. Although the detailed mechanisms responsible for the different outcomes are not well known, it is clear that glycaemic control during the first six weeks of organogenesis plays an important role in minimizing the risk for congenital malformations (5). Glycaemic control later in pregnancy seems to be important for other complications in the mother and child. During the past two-three decades, improved diabetes care in pregnancy has led to greatly reduced risk for several complications. However, although it is sometimes claimed that risks for severe complications similar to that in the background population can be achieved with pre-conception care and intensive follow-up, this goal has not been reached in practice (5,6).

Studying pregnancy outcome in women with diabetes presents a number of challenges. This includes varying criteria for and clinical practice in diagnosis, classification and detection of diabetes, varying target goals and clinical practice in treatment of women with diabetes, increasing occurrence of the different types of diabetes, and changing ethnic composition of the population. Classification of pre-gestational diabetes based on initial clinical characteristics is not always obvious, despite the recently introduced testing for antibodies to glutamic acid decarboxylase (7,8). Recent studies have shown that diabetes types other than pre-gestational type 1 diabetes are also associated with excess risk of several complications in mother and child (9-12).

THE MEDICAL BIRTH REGISTRY OF NORWAY AND DIABETES RESEARCH

The Medical Birth Registry of Norway (MBRN) has registered essentially all births in Norway since 1967, and diabetes is registered as a maternal diagnosis. This has been used in publications on pregnancy outcome in women with diabetes (13-16), and also studies of less well-established relations, such as those between perinatal factors and the risk of childhood onset type 1 diabetes based on registry linkage with the Norwegian Childhood Diabetes Registry (17-19), associations of type 1 diabetes associated genetic markers with size at birth (20,21), and intergenerational effects of diabetes in pregnancy (22,23). The first paper on pregnancy outcome in women with diabetes, by Jervell and co-workers in 1980, summarized the first years of operation of the MBRN (13), with a follow-up paper in 1994 (24). They reported that the perinatal mortality in offspring of mothers with pre-gestational diabetes fell dramatically from 1967-71 to 1987-1990. Vangen et al. included stratification by country of birth of the women (16). They reported that the overall perinatal mortality in Norwegian women with pre-gestational diabetes who gave birth during 1988-1998 was two-fold higher than in those without diabetes. Perinatal mortality in offspring of immigrant women with pre-gestational diabetes was similar to that of Norwegian women with diabetes, although the number of births among immigrants with diabetes limited the precision of the estimated risk. There has clearly been a substantial reduction in perinatal mortality and birth defects rates in pregnancies complicated by pre-gestational diabetes from the 1970s to the 1990s. However, it is too early to conclude that the rate of severe foetal and maternal complications in women with pre-gestational diabetes is equal to that of the background population in Norway. No publication has so far included births later than 1998, and the validity of the diabetes diagnosis needs to be addressed.

In 2000, BMJ published a paper comparing perinatal mortality and risk of congenital malformations in offspring of women with and without diabetes in Norway and north-east England, based on births 1994-1997 (25). This paper was retracted due to a technical error invalidating the results. In stead of including women with pre-gestational diabetes only, gestational diabetes was included and erroneously reported as pre-gestational diabetes. The retraction attracted some attention in the clinical and research community in Norway, but the fact that corrected data as well as new data from an independent study of the positive predictive value of the pre-gestational diabetes diagnosis were published with the retraction letter (26) seems to be less widely known.

In the remainder of this paper, we describe the diabetes data available in the MBRN and present two independent sets of data assessing the validity of the diabetes diagnosis in this registry.

CODING OF DIABETES IN THE MEDICAL BIRTH REGISTRY

Registration and coding practice are technical and may appear boring, but are essential for understanding how to use and interpret diabetes data in the MBRN. Users of data are encouraged to inspect the registration forms used (see e.g. MBRN annual report 2003-2004).

Births 1967-1998

Until 1988, diabetes mellitus was coded in the MBRN with an ICD-8 code 250 in the variable for maternal health before pregnancy. From 1988, additions of modified ICD-8 diabetes codes were recorded in the variable for maternal health during pregnancy, by adding an extra digit so that 2501 indicated insulin-treated or type 1 diabetes, 2502 indicated diet-treated or type 2 diabetes, 2503 indicated gestational diabetes (without information about diet or insulin), and 2509 indicated diabetes where type or treatment was not specified. Due to a space limitation in the field for diagnoses before pregnancy (three digits), these four-digit diagnoses were put in the field for maternal diagnoses during pregnancy, though they were often specifying pre-gestational diabetes. A diabetes code in the field for maternal diagnoses during pregnancy without the ICD-8 code 250 in the field for diagnoses before pregnancy identified gestational diabetes. Note that 2501 was used whenever insulin treatment before or during pregnancy was mentioned in the registration form, also in some cases where the woman had pre-gestational type 2 diabetes which was treated with insulin only during the pregnancy.

Of 723 pregnancies in the MBRN during 1998 with any diabetes code, pre-gestational diabetes was coded for 274 (code 250 before pregnancy, regardless of codes assigned in the field for maternal diagnoses during pregnancy). Among these 274, 37 were simultaneously coded in the field for diagnoses during pregnancy with insulin-treated diabetes (2501), 5 were simultaneously coded with diet-treated diabetes (2502), 119 had code 2509 (not classified), 93 did not have a diabetes code during pregnancy, and finally, 20 were simultaneously coded with 2503 during pregnancy (gestational diabetes, not further specified).

The current directions of the MBRN say that all diabetes codes during pregnancy (2501, 2502, 2503, 2509) that are not accompanied by simultaneous diabetes code of 250 before pregnancy should be taken as gestational diabetes. This was the case for 449 of the 723 pregnancies. Of these 449, 298 were coded with 2503 (gestational diabetes) during pregnancy, 45 were coded with insulin-treated gestational diabetes, 95 were coded with diet-treated gestational diabetes, and 11 were coded with 2509 during pregnancy (not specified type of treatment or type of diabetes).

Births 1999 to present

Since December 1998/January 1999, a new registration form with a number of changes was introduced.

This form has pre-coded boxes for type 1 diabetes before pregnancy, type 2 diabetes before pregnancy, gestational diabetes, and for glucosuria during pregnancy, respectively. An open field is available for specification of conditions present before or during pregnancy. For births registered with the new form, ICD-10 codes are used for diagnoses. ICD-10 diabetes codes reflecting information in the open field in the form are recorded in variables specifying maternal health before pregnancy (E10, E11, E13, E14, O24.0, O24.1, O24.3, O24.9) and during pregnancy (O24.4), respectively (although the ICD-10 code is not always used if the corresponding pre-coded diabetes box is ticked). In addition, a coding of insulin, A10a, has been used for maternal use of medication. According to the current directions from the MBRN, pre-gestational diabetes is defined when the box for type 1- or type 2 diabetes before pregnancy is ticked, or when one of the ICD-10 codes listed above, except O24.4 (gestational diabetes), is registered.

In 2004, 941 pregnancies were coded with some kind of maternal diabetes or insulin treatment. Of these, 234 were coded only with pre-gestational type 1 diabetes (box in form ticked), 108 were coded only with pre-gestational type 2 diabetes, 481 were coded with gestational diabetes only, while the remaining had either single codes that were non-specific or inconsistent combinations of codes (see Appendix 1 for details).

METHODS AND MATERIALS

Assessment of the positive predictive value of the diabetes diagnosis in the MBRN

The positive predictive value (PPV) is the proportion of all cases registered with diabetes in the MBRN who truly have diabetes. This was estimated using hospital medical records as the "gold standard". The medical records for women who had diabetes before or during pregnancy according to the MBRN and gave birth during 1998 in a total of 41 hospitals all over Norway were assessed by Narve Moe and other clinicians at the birth institutions (see Appendix 3 for list of hospitals). Altogether, 723 births were registered in the MBRN in 1998 with any diabetes code. The results of the medical record review was summarised in a standardised form specifying whether the woman had diabetes diagnosed for the first time during the relevant pregnancy (gestational diabetes), or whether diabetes was present before pregnancy (pre-gestational diabetes). Type 1 or type 2 was specified if sufficient information was provided. A brief summary of the results on pre-gestational diabetes was published in the letter to the editor of the BMJ in 2003 (26). Of the 723 births registered in the MBRN, the medical record was retrieved for 674, and the medical record was deemed conclusive by the clinician in 668 of these. Among the births where the medical record was conclusive, the MBRN had registered pre-gestational diabetes for 254

and gestational diabetes for 414. A separate review was done of medical records from women with diabetes codes in the MBRN who gave birth at Aker hospital in Oslo or one of 11 other hospitals (see Appendix 3) who were themselves born abroad (immigrants). Information about the country of birth was extracted from the medical records.

Assessment of the sensitivity of the diabetes diagnosis in the MBRN

The sensitivity of the diabetes diagnosis (often called ascertainment) is the proportion of true cases of diabetes in the mother that are coded as diabetes in the MBRN. To assess the sensitivity for pre-gestational type 1 diabetes, we linked persons with type 1 diabetes registered in the Norwegian Childhood Diabetes Registry to the MBRN, using the diabetes registry as the "gold standard". The Norwegian Childhood Diabetes Registry has prospectively registered all cases of newly diagnosed type 1 diabetes under the age of 15 years from 1989 (27). All diagnosed cases of type 1 diabetes in childhood are referred to the paediatric department at one of the county hospitals, and one paediatrician at each of these hospitals is responsible for notification to the registry (see Appendix 2 for a list of contributors). The day of the first insulin injection is used as the day of diagnosis. In addition, Geir Joner registered retrospectively all cases of type 1 diabetes with onset below age 15 years during 1973-1982 (28), as well as all cases diagnosed between age 15 and 29 years in the period 1978-1982 (29). Among persons with type 1 diabetes described above, women with known type 1 diabetes in the diabetes registry who gave birth in this period were identified by linkage to MBRN via the 11-digit personal identification number. The project was approved by the Norwegian Data Inspectorate and The Directorate for Health and Social Affairs. In the cohort of women with known pre-gestational type 1 diabetes in the Norwegian Childhood Diabetes Registry, 1025 births (by 606 mothers) were registered in the MBRN during 1976-1998, and 419 births (by 331 mothers) were registered between 1999 and 2004. The distribution of birth-years reflects the age-distribution of the women included in the diabetes registry and the years of operations, and does not represent the true occurrence of diabetes among all women who gave birth in the period covered. Ninety percent of the births occurred from 1985 and onwards, and 80% of the births occurred among women diagnosed before age 15 years.

RESULTS

Sensitivity of the pre-gestational diabetes diagnosis in the MBRN

Of births 1976-1998 among women with known pre-gestational type 1 diabetes, 97% were coded with pre-gestational diabetes in the MBRN (Table 1a). The

combination of codes used for births among women with known pre-gestational type 1 diabetes during 1999-2004 is shown in Table 1b. In this period, 94% were coded with pre-gestational diabetes according to the MBRN (first seven lines of Table 1b). Seventy-eight percent were correctly and uniquely coded with pre-gestational type 1 diabetes in the MBRN (Table 1b).

Positive predictive value of the gestational diabetes diagnosis in the MBRN for births during 1998

Among the 449 births coded by the MBRN as gestational diabetes, a conclusive hospital medical record was available for 414. The gestational diabetes diagnosis was confirmed in the medical record in 89% of the cases (Table 2). About one third of the incorrectly classified births were pre-gestational diabetes according to the medical record.

Positive predictive value of the pre-gestational diabetes diagnosis in the MBRN for births during 1998

Among the 274 births coded by the MBRN as pre-gestational diabetes, a conclusive hospital medical record was available for 254. The pre-gestational diabetes diagnosis was confirmed in 79.5% (Table 3), while more than half of births incorrectly classified by the MBRN were gestational diabetes according to the medical record review. Of the births classified as pre-gestational by the MBRN, 179 were pre-gestational type 1 diabetes and 23 were pre-gestational type 2 diabetes according to the medical record review. Because the information on type or treatment in this period was not sufficient to meaningfully classify pre-gestational diabetes as type 1- or type 2 diabetes (see section on coding above), positive predictive values could not be presented separately for type 1- and type 2 diabetes.

Medical records for immigrant mothers

Of the 91 births during 1998 reviewed for immigrant mothers coded with diabetes, the medical record was conclusive with regard to the diabetes diagnosis in 90. Twenty-three of these were born in Pakistan, 10 in Sri Lanka, 8 in India, 16 in Africa, 6 in the Middle East, 5 in Philippines, 5 in Vietnam, 3 in Turkey, one in Mexico, one in Chile, and 12 in Europe or the USA.

Of the 90 immigrant mothers, 67 had gestational diabetes according to the MBRN, of which 58 were confirmed by the medical record (86.6%, 95% confidence interval: 78.4%-94.7%). Of the 9 births incorrectly classified, 2 had pre-gestational type 2 diabetes and 7 had no mention of diabetes in the medical record.

Twenty-three immigrant women had pre-gestational diabetes according to the MBRN, of which 15 were confirmed in the medical record (65.2%, 95% confidence interval 45.8%-84.7%). Of the 15 with pre-gestational diabetes, 4 had type 1 diabetes and 11 had

Table 1a. Ascertainment (sensitivity) in the Medical Birth Registry of Norway 1976-1998 of pre-gestational type 1 diabetes.

Pre-gestational type 1 diabetes according to the Norwegian Childhood Diabetes Registry N=1025	Maternal diabetes diagnosis registered in the Medical Birth Registry of Norway		
	Pre-gestational diabetes	Gestational diabetes	No diabetes
	996 (97.2%)*	8 (0.8%)	21 (2.0%)

* The 95% confidence interval for the sensitivity was 96.2%-98.2%.

Table 1b. Diabetes diagnoses registered in the Medical Birth Registry of Norway 1999-2004 for 419 women with pre-gestational type 1 diabetes.

Pre-gestational type 1 diabetes according to the Norwegian Childhood Diabetes Registry	N=419
Diagnostic codes in the Medical Birth Registry of Norway	
Type 1 diabetes only	325 (77.6%)*†
Type 1 diabetes and gestational diabetes	43 (10.3%)*†
Unspecified diabetes (E14) before pregnancy	8 (1.9%)†
Type 1 and type 2 diabetes	1 (0.2%)*†
Type 2 diabetes only	14 (3.3%)†
Type 2 diabetes and gestational diabetes	1 (0.2%)†
Unspecified diabetes (E14) during pregnancy	1 (0.2%)†
Gestational diabetes only	7 (1.7%)
Insulin use during pregnancy only	5 (1.2%)
No code of diabetes or insulin use	14 (3.3%)

* MBRN type 1 diabetes: 369/419=88.1% (95% confidence interval 85.0%-91.2%)

† MBRN pre-gestational diabetes: 393/419=93.6% (95% confidence interval 91.5%-96.1%)

Table 2. Positive predictive value of a diagnosis of gestational diabetes in the Medical Birth Registry of Norway in 1998, on the basis of medical record review.

Medical Birth Registry	Medical record review		
	Gestational diabetes	Pre-gestational diabetes	No diabetes
Gestational diabetes (n=414)	370 (89.4%)*	16 (3.9%)†	28 (6.8%)

* The 95% confidence interval for the positive predictive value of the gestational diabetes diagnosis was 86.4%-92.3%.

† Nine of these had type 2 diabetes and 7 had type 1 diabetes before pregnancy, according to the hospital medical record review.

Table 3. Positive predictive value of a diagnosis of pre-gestational diabetes in the Medical Birth Registry of Norway in 1998, on the basis of medical record review.

Medical Birth Registry	Medical record review		
	Pre-gestational diabetes	Gestational diabetes	No diabetes
Pre-gestational diabetes (n=254)	202 (79.5%)*	32 (12.6%)	20 (7.9%)

* The 95% confidence interval for the positive predictive value of the pre-gestational diabetes diagnosis in the Medical Birth Registry of Norway (MBRN) was 74.6%-84.5%. Of the births classified by the MBRN as pre-gestational, 179 were pre-gestational type 1 diabetes and 23 were pre-gestational type 2 diabetes according to the medical record review.

type 2 diabetes according to the medical record. Among the 8 births incorrectly classified, 6 were gestational diabetes and for 2 there was no mention of diabetes in the medical record.

Assessment of coding errors

To get an impression of how the diabetes information written on the registration form is coded, and whether the written information is clearly interpretable, one of

us (IE) reviewed a random sample of 100 registration forms from 1998 with accompanying codes for diabetes. All hundred cases had some kind of diabetes information written in the form by the midwife or gynecologist. One case had a clear coding error, where gestational diabetes was coded as pregestational diabetes. Five cases had information about gestational diabetes in a previous pregnancy, of which three were coded with the ICD-8 code 250 for maternal health

before pregnancy (the other two were not coded with 250 before pregnancy, but were included in this review due to gestational diabetes in the current pregnancy). Two other cases had forms that were difficult to interpret, including one case where the only written information about diabetes was "diabetes matris" in the field for the baby's health, meaning that the baby was influenced by diabetes in the mother. In this case the mother was coded with unspecific diabetes during pregnancy (2509). In the other case "diabetes in the mother" in the space for conditions in the family (without clearly specifying whether this pertained to the birth giving woman or her mother) was interpreted as pre-gestational diabetes (code 250).

DISCUSSION

We have provided novel information on the validity of the diabetes diagnosis in the Medical Birth Registry of Norway (MBRN). Other important aspects such as complications associated with maternal diabetes, mechanisms behind the specific complications, screening for and treatment of maternal diabetes are all beyond the scope of this paper. Pregnancy outcome of births by women identified with pre-gestational type 1 diabetes by linkage of the Medical Birth Registry of Norway with the Norwegian Childhood Diabetes Registry will be presented elsewhere in the future.

Strengths and limitations

The assessment of the sensitivity for pre-gestational diabetes in the mother was established by registry linkage to a nation-wide diabetes registry (28-30). This was limited to type 1 diabetes with onset before age 15 in the majority of cases. A separate analysis of women diagnosed at age 15-29 indicated that the sensitivity was similar regardless of age at onset of pre-gestational type 1 diabetes (data not shown). Data were not available for validation of the sensitivity for pre-gestational type 2 diabetes. Another strength of the study was that an informative medical record was identified in the large majority of births coded with diabetes in the MBRN during one year, with essentially all birth institutions in Norway represented. However, the study of predictive value is limited by the quality of the information on diabetes in the medical record and by the fact that type 2 diabetes is underdiagnosed in the population (31,32). Medical records are likely to be less informative for the "mild" forms of gestational diabetes that are recommended to be treated by diet. Unfortunately, we have no data on the predictive value of the diabetes diagnosis in the MBRN for births after the introduction of a new registration form in 1999. The changes in the new registration form are likely to have influenced the validity to some extent, although this is currently not known. The prevalence of pre-gestational diabetes registered in the MBRN has increased in recent years.

This may as a whole reflect a true increase in the prevalence of diabetes among women giving birth. However, it is important in the future to study the predictive value of the diabetes diagnoses in the MBRN for births from 1999 and later.

Although we found a high ascertainment of type 1 diabetes in the MBRN, the estimated prevalence of pre-gestational diabetes in the MBRN during the 1990s (around 0.3-0.4%) is lower than the estimated prevalence of type 1 diabetes at age 30 years in the population (about 0.6%, based on the incidence 0-14 years in the 1990s (27), and the incidence 15-29 years during 1978-82 (29) in the Norwegian Childhood Diabetes Registry, and assuming negligible mortality). These data are not directly comparable, but the difference could be explained by a lower fertility rate among women with type 1 diabetes. This will be investigated and reported in a future study.

Types of misclassification

Of the births incorrectly coded with pre-gestational diabetes in the MBRN, a considerable proportion had gestational diabetes in the medical record, and vice versa. Evaluation of the coding practice revealed that "pure" coding errors were very rare. In 3 of 100 forms reviewed, notification of gestational diabetes in a previous pregnancy was coded with ICD-8 code 250 before pregnancy. Since there was no coding scheme to specify this scenario in the old registration form, the choice to use the diabetes code here may be regarded as technically correct, but it is inappropriate for most applications.

Furthermore, medical records sometimes only contained results of oral glucose tolerance test, without further information about symptoms and repeat testing. With changing and confusing diagnostic criteria, a certain proportion of errors (or lack of information) in both medical records and birth registration forms is probably inevitable.

Comparison with other studies

Detailed clinical information on each pregnancy should ideally have been available for studies of the outcome of pregnancy in women with diabetes, but given the relative rarity of both pre-gestational type 1 diabetes and the serious complications such as perinatal mortality and malformations, clinical studies are frequently too small, and one has to base studies on existing registries which often lack high-quality data on type of diabetes and metabolic control during pregnancy. Many such studies have been reported, see e.g. refs. (9,33,34) for recent publications, but few have validated the diabetes diagnoses adequately. In Sweden, women with maternal diabetes have been identified by record linkage to the Inpatient Registry, which is not complete and does not contain appropriate data on the type of pre-gestational diabetes (9,35). Their results for births in the 1980s indicated relative risks

slightly higher than those found in the MBRN (35). The validation of the Swedish Medical Birth Registry reported in 1990 (36) did not include an independent evaluation of the maternal diabetes diagnosis, but a more recent study has evaluated 184 medical records from women coded with gestational diabetes in the birth registry. They reported that 96.7% were correct (9), a figure slightly higher than what we have found for the MBRN.

Impact of misclassification

The impact of misclassification depends on the type and magnitude of misclassification, and on the intended use of the data. For instance, the observed results indicate that estimates of prevalence of diabetes is likely to be incorrect, but if the aim is to remove from analysis all of the births where the mother had pre-gestational type 1 diabetes, the data are probably suitable for the purpose. The positive predictive value of the pre-gestational diagnosis was moderate, and perhaps lower than could have been expected. On the other hand, as demonstrated by Hawthorne et al. (26), a misclassification in 20% of the cases would lead to a modest deflation of the relative risk for perinatal mortality and malformations. The observed perinatal mortality for Norway in the period 1994-1997 reported by Hawthorne et al. (26) was 7.2 per 1000 births among women registered without maternal diabetes and 15.6 per 1000 for mothers with pre-gestational diabetes, giving a relative risk of 2.17. The observed perinatal mortality rate of 15.6 for those coded with pre-gestational diabetes in the MBRN can be expressed as a weighted mean of the rate among the 20% incorrectly coded (assumed to be equal to that in the background population) and the unknown rate X among the 80% correctly coded births as follows: $0.8 \cdot X + 0.2 \cdot 7.2 = 15.6$. By simple algebra, we can work out that the unobserved rate among those with true pre-gestational diabetes under this scenario is 17.7 per 1000, corresponding to a relative risk of 2.46. Similar calculations by Hawthorne et al. showed that the relative risk for congenital malformations for women with pre-gestational diabetes was inflated from 1.3 to 1.4 by the misclassification. Similar calculations could also be

done for the impact of non-complete ascertainment. With a prevalence of pre-gestational diabetes less than 1%, a non-complete ascertainment would not influence these relative rates.

CONCLUSION

In conclusion, we have demonstrated a very good ascertainment of pre-gestational diabetes in the MBRN among women with type 1 diabetes. The new registration form introduced in 1999 allowed for specification of type of pre-gestational diabetes, but the predictive values of diabetes diagnoses are not known. For births during 1998 coded as pre-gestational diabetes and gestational diabetes according to the MBRN, approximately 80% and 90% were confirmed by medical records, respectively.

ACKNOWLEDGEMENT

Ingvild Eidem and Geir Joner were supported by a Ph.D.-grant from Eastern Norway Regional Health Authority (Ullevål University Hospital Trust). The authors would like to thank clinicians at all the birth institutions (listed in Appendix 3) involved in the review of medical records for invaluable help. Thanks also to Grace Egeland, Rolv Terje Lie, Jak Jervell, Sachiko Watanabe, and the staff at the Medical Birth Registry of Norway for assistance with various aspects of this study.

CONTRIBUTORS

NM contributed to the planning of the medical record review together with LMI, SV, and others. NM and other clinicians at the hospitals listed in Appendix 3 reviewed medical records retrieved from lists created by the MBRN (LMI). LMI summarized the conclusions based on medical review and assigned this information to the appropriate birth in the MBRN. Sachiko Watanabe punched this information into a database. SV reviewed medical records from immigrant mothers. GJ is the principal investigator for the project based on linkage of the Medical Birth Registry and the Norwegian Childhood Diabetes Registry. IE analysed the linked data and reviewed registration forms for coding errors, and drafted several text sections. LCS analysed the computerised data based on medical record review linked to the diabetes codes in the MBRN, and drafted the manuscript with input from all authors.

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Appendix 1. Combinations of diabetes or insulin codes used for births registered in the Medical Birth Registry of Norway during 2004.

Any diabetes or insulin code	N=941
Type 1 diabetes only	234 ‡
Unspecified diabetes (E14) before pregnancy	13 ‡
Type 1 and type 2 diabetes	4 ‡
Type 2 diabetes only*	108 ‡
Type 1 diabetes and gestational diabetes	48 ‡
Type 2 diabetes and gestational diabetes	35 ‡
Unspecified diabetes (E14) during pregnancy	2 ‡
Gestational diabetes only	481 §
Insulin use during pregnancy only	7
Gestational diabetes (O24.4) in a previous pregnancy only †	9

* Three of these were coded with the ICD-10 code E11 before pregnancy, the rest were only ticked for type 2 diabetes in the pre-coded box on the registration form.

† ICD-10 code O24.4 in mother's health before pregnancy. We assume that these cases represent gestational diabetes in a previous pregnancy. In total, 12 cases had such a code before pregnancy, three of them in combination with other diabetes codes.

‡ A total of 444 cases are counted as pre-gestational diabetes according to the current directions of MBRN. These include the cases with a code for gestational diabetes in addition to type 1 diabetes or type 2 diabetes and the cases coded E14 during pregnancy.

§ According to the directions from MBRN, these 481 are the total number of cases to be taken as gestational diabetes. Fifteen were coded with the ICD-10 code O24.4 during pregnancy, the rest were ticked for gestational diabetes in the pre-coded box on the registration form.

Appendix 2. Contributors to the Norwegian Childhood Diabetes Registry (Members of the Norwegian Childhood Diabetes Study Group).

Henning Aabech and Sven Simonsen, Fredrikstad; Helge Vogt, Lørenskog; Kolbeinn Gudmundsson, Anne Grethe Myhre, Knut Dahl-Jørgensen and Geir Joner, Oslo; Jon Grøtta, Elverum; Ola Tallerås and Dag Helge Frøisland, Lillehammer; Halvor Bævre, Gjøvik; Kjell Stensvold, Drammen; Bjørn Halvorsen, Tønsberg; Kristin Hodnekvam, Skien; Ole Kr. Danielsen, Arendal; Jorunn Ulriksen and Unni Mette Köpp, Kristiansand; Jon Bland, Stavanger; Dag Roness, Haugesund; Oddmund Søvik and Pål R. Njølstad, Bergen; Per Helge Kvistad, Førde; Steinar Spangen, Ålesund; Per Erik Hæreid, Trondheim; Sigurd Børsting, Levanger; Dag Veimo, Bodø; Harald Dramsdahl, Harstad; Bård Forsdahl, Tromsø; Kersti Elisabeth Thodenius and Ane Kokkvoll, Hammerfest.

Appendix 3. Births during 1998 registered with a diabetes code before or during pregnancy in the Medical Birth Registry of Norway (MBRN), by birth institution.

Hospital*	Births in 1998 registered with diabetes in the MBRN	Medical record retrieved
Østfold sentralsykehus†	30	28
Bærum sykehus†	10	9
Sentralsykehuset i Akershus†	29	25
Rikshospitalet†	41	34
Ullevål sykehus†	12	12
Aker sykehus†	107	106
Hamar sykehus	3	0
Hedmark sentralsykehus	10	0
Gjøvik fylkessykehus	2	2
Lillehammer fylkessykehus	10	9
Ringerike sykehus	1	1
Buskerud sentralsykehus†	27	26
Kongsberg sykehus	1	0
Vestfold sentralsykehus	15	15
Telemark sentralsjukehus	21	21
Aust-Agder sentralsjukehus	13	13
Flekkefjord sykehus	1	1
Vest-Agder sentralsykehus†	14	14
Fylkessjukehuset i Haugesund	25	25
Sentralsjukehuset i Rogaland†	60	59
Fylkesjukehuset på Voss	1	1
Fylkesjukehuset på Stord	6	0
Fylkesjukehuset i Odda	1	1
Haukeland sykehus	132	127
Fylkesjukehuset på Nordfjordeid	2	2
Fylkesjukehuset i Lærdal	1	1
Sentralsjukehuset i Sogn og Fjordane	15	14
Fylkesjukehuset i Molde	6	6
Fylkesjukehuset i Volda	5	5
Sentralsjukehuset i Møre og Romsdal	50	49
Fylkesjukehuset i Kristiansund	2	2
Orkdal Sanitetsforenings sjukehus	1	0
Regionsykehuset i Trondheim†	35	34
Innherred sykehus	3	3
Rana sykehus	1	0
Nordland sentralsykehus, Bodø	8	8
Stokmarknes sykehus	1	1
Regionsykehuset i Tromsø†	12	12
Kirkenes sykehus	3	3
Hammerfest sykehus†	3	3
Alta Helsesenter	3	2
Total	723	674

* Among a total of 41 hospitals, at least one medical record was retrieved from 35 hospitals. Narve Moe reviewed medical records at Østfold, Bærum, Akershus, Rikshospitalet, Ullevål, Aker (together with Siri Vangen), and Buskerud hospitals. Ole Jacob Nakling reviewed records at Lillehammer, Lars Johansen at Vestfold, Thyra Gæver at Telemark, Arild Kloster-Jensen at Aust-Agder, Aud Askvold at Vest-Agder, Eli Smedvik at Rogaland, Torunn Eikeland at Haugesund, Svein Rasmussen at Haukeland, Bjørg Ladehaug at Sogn og Fjordane, Sissel Hjelle at Møre og Romsdal, Bjørn Bache at Trondheim and Martin Grønberg at Tromsø.

† Hospitals included in separate review of immigrant mothers. Fifty-eight of 91 immigrant women from these 12 hospitals gave birth at Aker sykehus in Oslo.