Outcome of Pregnancy Among Immigrant Women With Diabetes

Siri Vangen, md[1,2]
Camilla Stoltenberg, phd, md[1]
Synne Holan, rn, rm[3]
Narve Moe, phd, md[2]
Per Magnus, phd, md[1]
Jennifer R. Harris, phd[1]
Babill Stray-Pedersen, phd, md[2]

OBJECTIVE — We studied outcome of pregnancy among immigrant women with diabetes. The women came from regions of the world with high incidence of impaired glucose tolerance and type 2 diabetes. Prevalences, secular trends, and sociodemographic risk factors of diabetes were also explored.

RESEARCH DESIGN AND METHODS — Data from the Medical Birth Registry of Norway on all births from 1988 to 1998 for mothers born in South Asia and North Africa (11,268) and Norway (601,785) were analyzed.

RESULTS — The prevalence of pregestational diabetes among the immigrants was 8.9/1,000 births, which was more than twice the rate among ethnic Norwegians (3.6/1,000). Time trends indicated increasing prevalences in both groups. Among the immigrants, diabetes was closely associated with maternal age. Maternal diabetes was associated with a significantly increased risk of pregnancy complications in both study groups. Increased risks were found for low birth weight, macrosomia, preterm birth, preeclampsia, and cesarean sections. Among ethnic Norwegians, maternal diabetes conferred a significantly increased risk of infant perinatal death (odds ratio 2.00, 95% CI 1,44–2.77). In the sample of immigrant women with predominantly type 2 diabetes, maternal diabetes was not significantly associated with perinatal death or congenital malformations in the offspring.

CONCLUSIONS — The high prevalence of diabetes among immigrants from South Asia and North Africa represents a challenge for health care providers. To prevent adverse pregnancy outcomes and later cardiovascular and renal morbidity among these groups, early diagnosis of diabetes, adequate metabolic control, and relevant preventive measures are warranted.

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There is global variation in the incidence of diabetes. The world's highest rates of type 1 diabetes are reported in Scandinavian countries (1), whereas high prevalences of impaired glucose tolerance and type 2 diabetes have been observed in countries in South Asia and North Africa (2). Although genetic predisposition plays an important role in the development of diabetes, the disease etiology is multifactorial. Factors such as age, diet, and obesity are central for the development of type 2 diabetes.

Diabetes increases the risk of pregnancy complications and adverse birth outcomes. Most of the research on pregestational diabetes and pregnancy outcomes has focused on type 1 diabetes (3,4). However, in many regions of the world, the number of pregnancies in women with type 2 diabetes is exceeding that of type 1 diabetes (5,6). Recent evidence suggests that type 2 diabetes is associated with fetal death and birth defects to the same extent as type 1 diabetes (7,8). The majority of immigrants in Norway are of Asian and African origin. Annually, there are about 800 births to women from the Indian subcontinent and North Africa in Norway. There are no previous published studies on diabetes prevalences and pregnancy outcomes among women with diabetes in these ethnic groups in Norway.

The main purpose of this study was to examine outcomes of pregnancy among immigrant women with diabetes. The women came from countries with high frequencies of impaired glucose tolerance and type 2 diabetes. Prevalences, secular trends, and sociodemographic risk factors of diabetes such as maternal age, parity, and maternal education level were also explored.

RESEARCH DESIGN AND METHODS

— The Medical Birth Registry contains information on all live births and stillbirths in Norway. Notification of all live births and stillbirths from the 16th week of gestation is mandatory, and information has to be sent to the Registry within 1 week after the delivery. A trained obstetric nurse completes a standardized form that contains information about the mother's health before and during the pregnancy, complications during delivery, and the condition of the child at birth. Linkage is established with the Population Registry and the Cause of Death Registry through the mother's unique identification number. These procedures ensure complete ascertainment of births and infant deaths. Linkage was also established with Statistics Norway to provide information about the maternal country of birth and education level.

Study population

The study population included a total of 613,053 births delivered in Norway from 1988 to 1998. Immigrant women from countries in North Africa and South Asia accounted for 11,268 of the births. The remaining births (601,785) were ethnic Norwegians. Initially, all analyses were

From the [1]Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway; the [2]Department of Obstetrics and Gynaecology, the National Hospital, Oslo, Norway; and the [3]Department of Obstetrics, Aker University Hospital, Oslo, Norway.

Address correspondence and reprint requests to Siri Vangen, Division of Epidemiology, Norwegian Institute of Public Health, PO Box 4404 Nydalen, N-0403 Oslo, Norway. E-mail: siri.vangen@fhi.no.

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performed for each population group separately. Inspection of the diabetes prevalence and associations between diabetes and birth outcomes in the different immigrant populations revealed similar rates, and therefore all the data for immigrants were pooled. The mean age of the study population was 27 years in both study groups (range: immigrants 15–52; ethnic Norwegians 12–50). Thirty-six percent of the immigrant women and 42% of the ethnic Norwegians delivered their first child. The majority (70%) of immigrants was living in Oslo or Bergen. The respective number for ethnic Norwegians was 22%. Many of the immigrants have attained Norwegian citizenship, but for simplicity, they will be referred to as immigrants without regard to citizenship. Births to second-generation immigrants are still very few in Norway, and these were not included.

Variables

Immigrants included all women residing in Norway who were born in Pakistan (5,775), Sri Lanka (2,441), India/Bangladesh (1,538), and Morocco/Algeria/Tunisia (1,154). Pregestational diabetes was defined as overt diabetes diagnosed before the pregnancy. The World Health Organization's diagnostic criteria for diabetes are used in Norway. Unfortunately, the Medical Birth Registry is not informative on the type of diabetes and the severity of the disease. Therefore, we performed a review of all medical records of women who visited the antenatal diabetes clinic at Aker hospital, the largest municipal hospital in Oslo, from 1992 to 1998. All women using insulin before the pregnancy were classified as having type 1 diabetes. A total of 43 women from the above-mentioned countries in Asia and Africa were diagnosed with manifest diabetes, and 12 of these women were using insulin before the pregnancy. Among ethnic Norwegians, 127 of 142 women with manifest diabetes were using insulin. If the results from this study are correct, ~70% of the immigrant mothers and 10% of ethnic Norwegians in our sample have type 2 diabetes. Around 50% of the immigrants and 30% of the ethnic Norwegians had a family member with diabetes.

Maternal age, defined as mother's age at delivery, was divided into four categories: <25, 25–29, 30–34, and >34 years. Parity was coded into three levels: first, second, and third pregnancy or higher. Mother's educational level was categorized as <10, 10–12, >12 years, and missing information. The place of delivery was categorized as the counties of Oslo/Hordaland versus elsewhere in Norway. The dichotomy Oslo/Hordaland was chosen as a method to test for regional differences because diabetes was recorded more frequently in Oslo and Hordaland counties than elsewhere in the country.

The pregnancy outcomes studied here include low birth weight, macrosomia, preterm birth, preeclampsia, operative vaginal delivery, shoulder dystocia, cesarean section, congenital malformations, and perinatal deaths. Due to differences in mean birth weights between the immigrants and ethnic Norwegians, the birth weight variables were defined according to population-specific birthweight distributions. Low birthweight was defined as 2 SDs below the population-specific mean value. Macrosomia was defined as 2 SDs above the population-specific mean value. Preterm birth was defined as gestational age <37 weeks. Data in the Medical Birth Registry have been coded according to the ICD. The 8th revision (ICD-8) was used during the study period. Preeclampsia was defined as a combination of proteinuria and hypertension. Operative vaginal delivery included delivery by forceps or vacuum. Shoulder dystocia was defined as difficulty delivering the baby's shoulders due to large body stature. Cesarean section included elective and acute surgery. Congenital malformations represented a pooled category, including all severe birth defects. Perinatal deaths included deaths during pregnancy, delivery, or within the first week of life. The World Health Organization's criterion for fetal death was applied: death of a fetus of gestational age ≥22 weeks or birthweight ≥500 g.

Validation of data

To validate the diabetes data in the Norwegian Medical Birth Registry, information was extracted from the Registry about all women with diabetes who delivered at 13 hospitals in the counties of Oslo, Akershus, Østfold, Buskerud, Trøndelag, Rogaland, Vest-Agder, and Finnmark during 1998. These pregnancies were identified and compared with information in the medical records. For pregestational diabetes, information in the Registry was in accordance with the medical records. Gestational diabetes, however, was over-recorded, as 4 of 40 (10%) cases among the immigrants and 48 of 153 cases (30%) among ethnic Norwegians with risk factors of the disease had been registered as gestational diabetes cases.

Statistical analyses

Cross tabulation was used to calculate prevalences and secular trends of diabetes. Odds ratios with 95% CIs for associations of maternal age, parity, maternal educational level, and pregnancy outcomes with diabetes were estimated with logistic regression analyses. Computation was performed with SPSS software release 10.0.

RESULTS

Prevalences and sociodemographic risk factors

A high prevalence of pregestational diabetes was found among the immigrants, with rates greater than twice that found among ethnic Norwegians (Table 1). Among immigrants, the risk of pregestational diabetes was closely associated with maternal age (Table 2). For women aged >34 years, the risk was six times higher than for women aged <25 years. These relative risk associations remained unchanged after adjusting for parity, maternal education, and place of delivery. No independent effect was observed for parity or education level on the risk of developing gestational diabetes. Among ethnic Norwegians, there was no such effect of maternal age, but high education level was associated with a lower risk of diabetes in this group.

The median maternal age of nulliparous immigrant women increased from 24 to 25 and from 25 to 27 years among immigrants and ethnic Norwegians, respectively, during the study period (data not shown).

Pregnancy outcomes

Maternal diabetes was associated with considerably increased perinatal risks and conferred a greater than threefold increase in risk of macrosomia, preterm birth, preeclampsia, and cesarean section in both study groups (Table 3). The risk of macrosomia in offspring of immigrant mothers with diabetes was particularly high and elevated by a factor of more than five compared with women without dia-

Table 1—*Ethnic comparison of pregestational diabetes over time, Norway 1988–1998*

	Immigrants*				Ethnic Norwegians			
Period	Births (*n*)	*n*	Per 1,000	95% CI	Births (*n*)	*n*	Per 1,000	95% CI
1988–1990	2,549	20	7.8	4.8–12.1	165,715	488	2.9	2.7–3.2
1991 and 1992	1,995	17	8.5	4.9–13.6	111,695	373	3.3	3.0–3.7
1993 and 1994	2,013	17	8.5	4.9–13.5	109,389	414	3.8	3.4–4.3
1995 and 1996	2,248	20	8.9	5.4–13.7	109,427	433	4.0	3.6–4.3
1997 and 1998	2,463	26	10.6	6.9–15.4	105,559	485	4.3	4.2–5.0
Total	11,268	100	8.9	7.2–10.6	601,785	2,166	3.6	3.5–3.8

*Women born in Pakistan, India, Bangladesh, Sri Lanka, Morocco, Tunisia, and Algeria.

betes. Increased risks (approximately doubled) were also found for low birthweight and low Apgar scores in both study groups. Among immigrant mothers, diabetes was not significantly associated with perinatal death and congenital malformations in the offspring.

CONCLUSIONS

Main findings

Diabetes is a common complication in pregnancy among ethnic minority women from South Asia and North Africa. The majority of immigrant women with pregestational diabetes had type 2 diabetes. Pregestational diabetes was associated with a considerably increased risk of adverse birth outcomes in both study groups, including low birthweight, macrosomia, shoulder dystocia, preterm birth, preeclampsia, cesarean section, and low Apgar score. Offspring perinatal death or congenital malformations was not significantly associated with maternal diabetes among the immigrant women. Among ethnic Norwegians, maternal diabetes conferred a doubled increased risk in offspring perinatal death.

Methodological considerations

The missing information on maternal weight and height in the Birth Registry pose important limitations in our analyses. The results in the Tables 1 and 2 may be confounded by maternal obesity that is likely to increase with age. Results from the study at Aker hospital showed that 42% of immigrant women had a BMI >30 kg/m^2 and suggest that obesity is important for the development of diabetes in this group. The corresponding number for ethic Norwegians was 12%.

We also explored prevalences and pregnancy outcomes for women with gestational diabetes. A very high prevalence was found among the immigrants (31.9/1,000 births), which was seven times higher than that among ethnic Norwegians (4.5/1,000). Associations of gestational diabetes with pregnancy outcomes

Table 2—*Impact of maternal age, parity, education, and place of delivery on risk of pregestational diabetes among immigrants in Norway, 1988–1998*

	Immigrants*: pregestational diabetes (n = 100)			Ethnic Norwegians: pregestational diabetes (n = 2,166)		
		Adjusted†			Adjusted†	
Measure	Per 1,000	OR	(95% CI)	Per 1000	OR	(95% CI)
Maternal age (years)						
<25	3.0	1.00		3.19	1.00	
25–29	6.0	1.88	(0.88–4.02)	3.98	1.33	1.19–1.48
30–34	13.6	4.32	(2.03–9.20)	3.47	1.24	1.08–1.42
>34	23.3	7.19	(3.23–6.00)	3.60	1.30	1.09–1.55
Parity						
p0	5.2	1.00		3.72	1.00	
p1	8.3	1.12	(0.62–2.03)	3.88	1.00	0.91–1.11
p > 1	13.3	1.13	(0.63–2.01)	2.93	0.75	0.65–0.85
Education (years)						
0–9	9.4	1.00		4.07	1.00	
10–12	7.8	0.89	(0.45–1.76)	3.72	0.88	0.76–1.03
>12	13.0	1.15	(0.51–2.56)	3.27	0.68	0.58–0.81
Missing information	9.2	1.06	(0.59–1.89)	2.82	0.70	0.33–1.49
Place of delivery						
Oslo and Hordaland	9.8	1.00		5.64	1.00	
Other places	6.7	0.71	(0.44–1.15)	3.00	0.53	0.48–0.58

*Women born in Pakistan, India, Bangladesh, Sri Lanka, Morocco, Tunisia, and Algeria. †Adjusted for maternal age, parity, educational level, and place of delivery. p0, first pregnancy; p1, second pregnancy; p > 1, third pregnancy or more.

Table 3—*Ethnic comparison of pregnancy outcomes (%) for mothers with and without diabetes, Norway 1988–1998*

	Immigrants*				Ethnic Norwegians			
	Diabetes (n = 100)	No diabetes (n = 11,168)	OR†	95% CI	Diabetes (n = 2,166)	No diabetes (n = 599,619)	OR†	95% CI
Low birthweight	11.0	4.1	2.62	1.37–4.99	8.9	4.2	2.10	1.80–2.43
Macrosomia	13.0	2.0	5.54	3.00–10.23	5.7	1.7	3.82	3.18–4.59
Preterm birth (<37 weeks)	25.0	10.0	3.08	1.92–4.93	20.9	6.4	3.75	3.38–4.17
Preeclampsia	9.0	2.2	3.58	1.76–7.29	14.7	3.5	4.68	4.14–5.29
Shoulder dystocia‡	3.2	0.9	2.45	0.59–10.24	2.4	0.7	3.39	2.57–4.49
Operative vaginal delivery	6.0	8.3	0.59	0.41–0.83	10.2	7.4	1.36	1.18–1.57
Cesarean section								
Total	37.0	14.7	3.08	2.02–4.71	47.5	12.3	6.47	5.93–7.05
Elective	12.0	5.0	2.08	1.12–3.86	24.1	4.4	6.87	6.21–7.61
Apgar score <7 at 5 min	4.0	1.7	2.18	0.79–6.03	2.8	1.3	2.21	1.71–2.86
Congenital malformations	1.0	2.5	0.36	0.05–2.69	3.0	2.3	1.21	0.94–1.55
Perinatal deaths	2.0	1.3	1.47	0.36–6.09	1.8	0.9	2.00	1.44–2.77

*Women born in Pakistan, India, Bangladesh, Sri Lanka, Morocco, Tunisia, and Algeria. †The odds ratios were adjusted for maternal age, parity, education level, and place of delivery. ‡Vaginal births only.

showed a similar but less severe risk pattern than that seen for pregestational diabetes. However, for gestational diabetes, there was no association with congenital malformations or perinatal deaths. Due to the nonvalid registration, the data about gestational diabetes was removed from the tables.

Among immigrants, the small number of cases for some of the outcomes (for example, preeclampsia in Table 3) may involve a disproportionate number of women with type 1 diabetes. Thus, the conclusion cannot be draw that type 2 diabetes is associated with these outcomes.

Time trends and sociodemographic factors

Impaired glucose tolerance and type 2 diabetes are prevalent among populations of the Indian subcontinent (9). Migration from rural areas to cities with a more sedentary city life and increased energy density of diets has lead to a threefold increase of the disease (10,11). The high prevalence of type 2 diabetes in urban areas of South Asia is comparable to that of migrant populations residing in Europe (10–12). The prevalence of diabetes among the immigrants in the current study was more than doubled and the prevalence of gestational diabetes seven times greater compared with ethnic Norwegians. The causes for these differences are not clear, and both environmental and genetic factors have been considered. The fetal origin hypothesis purports that the in utero environment, particularly maternal undernutrition, may program later risk of diabetes (13). One could therefore predict that its incidence would fall as nutrition in a population improves. Geneticists have ascribed insulin resistance to a "thrifty gene" and hypothesize that the populations in the developing world have been selected for ability to survive periods of starvation. When there is access to food and physical activity declines, they develop diabetes, hypertension, and coronary heart disease (14). Research among Pima Indians of Arizona showed that offspring of women who had diabetes during pregnancy were more obese and had a higher prevalence of type 2 diabetes (15). The exposure to the diabetic intrauterine environment was responsible for ~40% of all type 2 diabetes in Pima Indian adolescents. Thus, the diabetic pregnancy has consequences for the offspring far beyond the neonatal period. In light of these factors, we would expect the diabetes prevalence to increase among future generations of South Asian and North African immigrants.

Maternal age was a strong predictor of diabetes among the immigrant women. For this group, there is a shift toward higher age of childbearing compared with the situation in their country. A shift in childbearing age was also observed during the study period in the current study. The increasingly older ages at which women start their childbearing period may also contribute to increasing prevalences of diabetes. Joner and Søvik (16) reported that the incidence of type 1 diabetes in the group aged 15–29 years doubled from 1960 to 1980 in Norway. Joner and Søvik also reported marked geographical differences in diabetes incidence. These findings are congruent with the observations in the current study pointing to the operation of environmental pathogenic factors.

The association between diabetes and socioeconomic factors may vary between populations and over time. In the current study, high education level was associated with lower risk among the ethnic Norwegian women. Such a situation has also been described in an early study from Denmark (17). Among the immigrants, however, there was no clear association between education level and diabetes. A study of diabetes among South Asian inhabitants of The Hague reported a higher prevalence in the lowest socioeconomic strata in the group aged 31–49 years. In the age-group >60 years, the prevalence of diabetes did not differ between the higher and lower socioeconomic strata (18).

Outcomes of pregnancy

Macrosomia is a well-known complication of diabetes in pregnancy. Maternal glucose levels influence fetal growth (19). Increased levels stimulate fetal insulin secretion and fetal growth with subsequent neonatal macrosomia. It has been hypothesized that perceptions of type 2 diabetes as "mild diabetes" might result in poorer attendance for pregnancy care, later booking for antenatal clinic, and poor gly-

cemic control (20). Both maternal hyperglycemia and maternal obesity increase birthweight within a given population (19,21). Fetal macrosomia was elevated by a factor of more than five among the immigrant women with diabetes as compared with those with no diabetes. This finding may implicate suboptimal glycemic control. However, the results from the mini-audit showed that the 43 immigrant women who attended the antenatal diabetes clinic at Aker hospital were enrolled in the first trimester and attended weekly until delivery, which is generally practiced for women with diabetes in Norway. Elevated HbA_{1c} (>6.4%) was found among 73% of the immigrant women at the first antenatal visit. By the time of the delivery, the proportion of women with elevated HbA_{1c} was reduced to 35%. The respective number among ethnic Norwegians was 70 and 33%. This indicates that the success of treatment was similar in both groups. However, the relatively larger proportion of macrosomia among the immigrant mothers compared with ethnic Norwegians may be due to larger glycemic fluctuations, with high levels triggering the fetal growth. An additive effect of diabetes and obesity may also play a role and highlights the importance of interventions to reduce obesity among the immigrant women.

It has been proposed that the high risk of preterm delivery in women with diabetes is an iatrogenic effect of active obstetric management with frequent use of cesarean section (4). In the current study, diabetes was associated with a three times greater risk of preterm delivery in both study groups. This risk persisted when only births with spontaneous onset were included in the analyses. This finding is congruent with other studies and offers support for the hypothesis that metabolic disturbances associated with diabetes are etiological factors leading to preterm delivery (22).

Maternal diabetes increases the risk of preeclampsia, and the risk increases with the severity of the metabolic disturbance (23). The results of the current study showed a considerable increased risk of preeclampsia among women with diabetes as compared with those with no diabetes. It has been reported that superimposed preeclampsia in women with diabetes increases the risk of other adverse birth outcomes, including preterm birth, intrauterine growth restriction, and delivery by cesarean section (24). Our data supported these last findings: low birthweight and preterm birth occurred in 19 and 41%, respectively, in the total sample of diabetic pregnancies complicated with preeclampsia, and 78% of these pregnancies were delivered by cesarean section.

Recent clinical studies of hospital populations have reported that the risks of offspring perinatal death and of congenital malformations are similar regardless of the whether women have type 1 or type 2 diabetes (7,8). In the current study, diabetes among the immigrants, which was predominantly type 2 diabetes, was not significantly associated with offspring perinatal death or birth defects. The relatively small sample may play a role here. The contrasting results may also be related to the criteria used in the various studies to define diabetes cases. The current study was population based and included all diabetes cases, as opposed to clinical studies that may be restricted to cases with a more severe metabolic disturbance and, consequently, a higher risk of adverse outcomes. Varying socioeconomic conditions in the population studied, lack of maternal awareness, late presentation for antenatal care, and delayed diagnosis could also play a role. It has also been postulated that the severity of the metabolic disturbance rather than the type of diabetes affect the risk of birth defects and perinatal death (8,25). There is evidence that this is also the case for a range of other perinatal outcomes. Thus, antenatal care for mothers with diabetes and success of treatment to control metabolic disturbances has a powerful impact of the perinatal outcome. Even though care for mothers with diabetes has a high priority within the Norwegian health care system, the HbA_{1c} estimates from the study at Aker hospital indicated suboptimal glycemic control for a substantial number of women in both study groups by the time of delivery. This indicates that there is still a potential for improvement.

Implications for health care providers

Type 2 diabetes and impaired glucose tolerance are widespread among immigrants from South Asia and North Africa. Our findings represent a challenge for health care providers in early diagnosis of diabetes, adequate metabolic control, and relevant information. There is evidence that ~60% of women with gestational diabetes will develop manifest diabetes within 16 years (26). Women with gestational diabetes should therefore undergo regular metabolic control in the years after the delivery. To prevent development of diabetes and cardiovascular and renal morbidity and mortality at a later age, preventive measures including dietary advice, particularly on restricting carbohydrates and regular physical activity, are warranted.

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