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The associations between nationality, fertility history and diabetes-related mortality: a retrospective cohort study in the Brussels-Capital Region (2001–2005)

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ABSTRACT

Background The relationship between women's parity and diabetes mortality has been investigated in several studies, with mixed results. This study aims to establish if parity and age at first birth are associated with diabetes-related mortality and if these factors contribute to variations in diabetes-related mortality among women with different nationalities.

Methods Data of the 2001 census are linked to registration records of all deaths and emigrations (period 2001–2005). The study population comprises all female inhabitants of the Brussels-Capital Region aged 45–74 of either Belgian or North African nationality ($n = 108\,296$). Age-standardized mortality rates (direct standardization) and mortality rate ratios (Poisson's regression) are computed.

Results Both parity and age at first birth are associated with diabetes-related mortality. Highest risks of dying from diabetes are observed among grandmultiparous women and teenage mothers. Differences in diabetes-related mortality according to nationality are observed. Age-standardized diabetes mortality rates are higher in North African [ASMR = 417.4/100 000; 95% confidence interval (CI) 227.2–607.7] than in Belgian women (ASMR = 184.0/100 000; 95% CI 157.3–210.8). Taking parity, age at first birth and education into account, these differences largely disappear.

Conclusions Reproductive factors are associated with diabetes-related mortality and play an important part in the higher diabetes-related mortality of North African compared with Belgian women.

Keywords ethnicity, diabetes, mortality

Introduction

There is much evidence that diabetes morbidity differs between ethnic groups. These ethnic differences are only in part explained by conventional risk factors and socioeconomic characteristics.[1,2] Previous studies also indicate that diabetes mortality rates vary between ethnic groups.[2–4] Explanations for ethnic variability in diabetes mortality are not well established, although ethnic diversity in both diabetes risk factors (genetics and lifestyle) and in diabetes management (metabolic control and access to and quality of health care) may play a part.[5,6] Higher diabetes morbidity and mortality rates are observed in people of North African origin compared with people of European origin.[1,3]

Although parity is not a conventional risk factor for diabetes, recent research suggests an association between parity and both diabetes morbidity and mortality. Regarding diabetes morbidity, results have been inconsistent. Some studies find a positive association between parity and diabetes morbidity;[7] other studies observe increased diabetes morbidity among nulliparous women[8] and yet others identify

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grandmultiparous women as a high-risk group.[9] Most research on parity and diabetes mortality shows increased diabetes mortality risk among nulliparous and grandmultiparous women.[10,11] Furthermore, an association between parity and cardiovascular morbidity and mortality is found.[12,13]

To our knowledge, the relationship between timing of fertility and diabetes (mortality) has not yet been examined. However, there are indications that adolescent mothers are at increased risk of subsequent obesity[14] and have higher all-cause mortality.[15] A recent study shows that teenage mothers have an excess mortality from a number of causes including cardiovascular mortality.[13]

Overall, reproductive behaviour is considered to have a long-term impact on women's health and mortality.[15] There are a number of mechanisms, which may underlie this association. These mechanisms can be categorized under *causal mechanisms* and *selection effects*. The first category comprises (direct) physiological effects of childbearing as well as more (indirect) biosocial consequences of childrearing, such as role changes and stress associated with motherhood and increased social control of unhealthy behaviour.[16] The second category includes selection effects. Selection may play an important part, as socioeconomic characteristics (e.g. education) are strongly associated with both fertility behaviour[16,17] and health and mortality.[16,18] Likely, causation as well as selection contributes to the association between reproductive factors and mortality.

Reproductive behaviour is also related to ethnic origin. A recent UK study shows that the age profiles and fertility levels differ greatly between ethnic groups.[19] In Belgium, women of North African origin have higher fertility and are generally younger at first childbirth, although fertility patterns have changed substantially in recent decades.[20]

The objectives of this study are to examine if parity and age at first birth are associated with diabetes-related mortality in the Brussels-Capital Region (BCR) and if these reproductive factors partly account for the higher diabetes-related mortality of North African women compared with Belgian women.

Methods

Design and study population

The setting of this research was the BCR. The reason for focusing on this region was 2-fold. First, its metropolitan profile provided us with a context that was particularly suited to examine ethnic variations. In 2001, 48.3% of the BCR population was of foreign origin, with the population of North African origin being most represented (14.6% of BCR population) (Belgian 2001 census). Second, the BCR mortality data were the only census-linked mortality data available for Belgium at the moment.

Data were derived from record linkage between the Belgian census and emigration and mortality data. In a first stage, a direct link between the 2001 census and register data of all deaths and emigrations in the period 1 October 2001–1 January 2005 was established by Statistics Belgium. In this way, numerator–denominator bias was avoided. In a second stage, cause-specific mortality data were added by the first author using anonymous individual linkage with death certificates. This linkage was based on a 'key', consisting of a number of variables that were available in the census/register as well as in the death certificates (date of birth, date of death, sex and municipality of residence). A unique match could be found for 81.5% of all deaths. For the remaining 18.5%, probabilistic linkage methods were applied. Using this two-stage linking procedure, a match was established for 92.3% of the people registered at the time of the census and dying during the observation period. The main reason for non-matching was missing death certificates due to mortality abroad. Consequently, there were more people of foreign origin for whom no match could be found (12.9% versus 6.6% among people of Belgian origin).

The study population consisted of Belgian and North African women aged 45–74 living in the BCR ($n = 108\,296$). The lower age limit was 45 years in order to include mostly women who had completed their childbearing. Above 74 years of age, the number of women of North African origin older than 74 was very small ($n = 404$). This study focuses on differences between women of Belgian and North African origin, as the North African community is the largest (non-western) ethnic group in the BCR (14.6% of BCR population, whereas the second largest non-western community, the Turks, makes up only 3.9% of population). Other ethnic groups were excluded from the analyses.

Variables

Mortality from diabetes was determined by ICD-10 codes E10–E14. To capture the actual burden of diabetes, both death certificates with diabetes as an underlying cause of death and with diabetes as one of the causes of death (any mention of diabetes) were analysed. The independent variables were based on information available in the 2001 census. The variable *age* was included as a categorical variable (5-year age bands) in the direct standardization analyses and as a continuous variable in the Poisson regression analyses. Nationality was used as a proxy for *ethnicity*. To

maximize the number of women of North African origin, information on current nationality and nationality of birth was combined. If either current nationality or nationality of birth was Algerian, Egyptian, Libyan, Moroccan or Tunisian, people were considered as being of North African origin. Reproductive factors included in the analyses were parity and age at first birth. *Parity* was divided into six categories: 0, 1, 2, 3, 4–8 and ≥9 live births. *Age at first birth* was classified into five age groups: <18, 18–25, 25–30, 30–35 and ≥35. Several sensitivity analyses using different classifications of parity and age at first birth were also carried out (cf. infra). As socioeconomic position is strongly associated with both fertility behaviour and mortality, education (as an indicator of socioeconomic position) was entered into the analyses. *Educational attainment* was categorized according to the International Standard Classification of Education (ISCED). The educational levels are (ISCED 0) pre-primary education; (ISCED 1) primary education; (ISCED 2) lower secondary education; (ISCED 3) upper secondary education and (ISCED 4–6) tertiary education.[21]

Data analysis

The χ^2 test of independence (categorical variables) and the unpaired *t*-test (continuous variables) were used to compare background characteristics between Belgian and North African women. To obtain an overview of differences in diabetes mortality according to nationality, age-standardized mortality rates (ASMRs) were computed for each nationality group, directly standardized to the 45- to 74-year-old female Belgian population of the BCR. Both ASMRs for diabetes as the underlying cause of death (*diabetes mortality*) and for diabetes as one of the causes (*diabetes-related mortality*) were calculated. Since risk of dying from diabetes is small and the time span studied is relatively short (implying approximately constant hazard rates during the study period), the Poisson regression was carried out. The Poisson regression models using conventional (observed information matrix) variance method were applied to examine relative differences in diabetes-related mortality between Belgian and North African women. The dependent variable in these analyses was diabetes-related mortality in order for statistical power to be maximized. The independent variables were nationality group, parity, age at first birth and educational attainment. To challenge the robustness of the findings, several sensitivity analyses were performed. First, the Poisson regression was carried out with different categorizations of nationality group, parity and age at first birth. Second, as previous research has shown an association between various reproductive factors and cardiovascular disease (CVD) and mortality,[12,13] sensitivity analyses that take cardiovascular deaths into account were performed. All analyses were adjusted for age and performed using Stata 11.

Results

Participants

Of all women included at baseline ($n = 108\,296$), 98 380 were of Belgian and 9916 of North African origin. During the follow-up period, 3463 women died and 574 migrated out of the BCR.

Baseline characteristics—measured at the 2001 census—differed strongly by nationality (cf. Table 1). North African women were generally less educated, had more children and were younger at childbirth than Belgian women.

An inverse gradient was observed between educational attainment and diabetes-related mortality. Age-adjusted diabetes-related mortality rate ratios (MRRs) for pre-primary, primary, lower secondary, upper secondary and tertiary education were: 1.00 (ref.), 0.87 [95% confidence interval (CI) 0.55–1.37], 0.44 (95% CI 0.27–0.71), 0.41 (95% CI 0.24–0.69) and 0.14 (95% CI 0.06–0.29), respectively.

Burden of diabetes mortality

In the period 2001–2005, 40 women died of diabetes as the underlying cause of death. In the same period, the number of diabetes-related deaths was more than five times higher ($n = 207$). North African women have higher ASMRs compared with Belgian women. As for diabetes-related mortality, the ASMR for North African women amounted to 417.4/100 000 (95% CI 227.2–607.7), whereas the ASMR for Belgian women was 184.0/100 000 (95% CI 157.3–210.8)/100 000 (cf. Table 2).

Pregnancy-related risk factors

Grandmultiparous women had higher diabetes-related mortality, e.g. the MRR for women with four to eight children relative to women with two children amounted to 2.40 (95% CI 1.56–3.70) (cf. Table 3). Age at first birth was strongly related to diabetes-related mortality. A particularly high diabetes-related mortality was observed in women who were younger than 18 at first birth ($MRR_{<18 \text{ versus } 25-30} = 7.48$; 95% CI 4.20–13.34). Moreover, women aged 18–25 at first childbirth also had relatively high diabetes-related mortality.

When both reproductive factors were taken into account, the relative differences in diabetes-related mortality by parity and age at first birth attenuated but remained substantial (Model 3). In Model 4, the mortality analysis was also adjusted for educational attainment. Again, MRRs were slightly lower,

Table 1 Baseline socio-demographic and reproductive factors according to nationality

	Belgian origin, mean/n (SD/%)[a]	*North African origin, mean/n (SD/%)*[a]	*t/χ^2 statistic (d.f.)*[b]	*P-value*
Socio-demographics				
Age (years)	59.5 (8.9)	55.0 (7.9)	$t = 48.6$ (108 294)	<0.0001
Educational level (cat.)[c]			$\chi^2 = 38\,000$ (4)	<0.0001
Pre-primary	3343 (3.8)	5530 (69.3)		
Primary	14 539 (16.3)	1107 (13.9)		
Lower secondary	25 219 (28.4)	795 (9.9)		
Higher secondary	19 409 (21.8)	360 (4.5)		
Tertiary	26 394 (29.7)	189 (2.4)		
Reproductive factors				
Parity (cat.)[c]			$\chi^2 = 28\,000$ (3)	<0.0001
0	15 705 (17.5)	469 (5.5)		
1	25 820 (28.8)	562 (6.6)		
2	27 724 (30.9)	685 (8.0)		
3	12 609 (14.1)	822 (9.7)		
4–8	7752 (8.6)	4901 (57.6)		
≥9	107 (0.1)	1076 (12.6)		
Age at first birth (cat.)[c]			$\chi^2 = 65\,000$ (4)	<0.0001
<18	1850 (2.5)	1647 (20.8)		
18–25	39 558 (53.7)	4560 (57.5)		
25–30	22 537 (30.6)	1019 (12.8)		
30–35	7137 (9.7)	390 (4.9)		
≥35	2578 (3.5)	317 (4.0)		

[a]For continuous variables, unpaired *t*-tests are used to compare Belgian and North African women. Means and standard deviations (SD) are presented. If the variable is categorical, χ^2 tests are performed. Numbers of subjects (*n*) and percentages are presented.
[b]d.f., degrees of freedom.
[c]cat., categorical variable.

but grandmultiparous women and teenage mothers continued to have higher risk of dying from diabetes.

Differences in diabetes-related mortality by nationality

North African women had higher diabetes-related mortality relative to Belgian women (MRR = 2.96; 95% CI 1.90–4.60) (cf. Fig. 1, series 1). When parity was taken into account (Model 2), 60% of the excess diabetes-related mortality among North African women was explained. If the analyses were adjusted for parity and education (Model 3), the mortality rate of North African women was only 1.27 times that of Belgian women (95% CI 0.67–2.44).

Subanalyses among parous women were conducted (n = 82 057; N_{MCOD} = 165) (cf. Fig. 1, series 2). When parity and age at first birth were included in these analyses (Model 2), the MRR for North African versus Belgian women dropped from 2.95 (95% CI 1.87–4.65) to 1.43 (95% CI 0.80–2.57). Hence, these reproductive factors largely accounted for the higher diabetes-related mortality among parous North African women. If the mortality analysis was also adjusted for education (Model 3), differences in diabetes-related mortality by nationality largely disappeared (MRR = 1.12; 95% CI 0.56–2.23).

To inquire into the solidity of the findings, sensitivity analyses were also carried out. Using different categorizations of nationality group, parity or age at first birth resulted in similar findings. Further analyses were performed among women who died from diabetes as one of the causes of death. These women were divided into two groups: (i) women with any mention of CVDs (ICD-10: codes I00–I99) on their death certificates; and (ii) women with no mention of CVDs. In both subgroups, the associations between parity, age at first birth and diabetes-related mortality remained.

Discussion

Main findings of this study

This study lends support to hypotheses *linking reproductive factors to diabetes-related mortality* among women.

Table 2 Number of diabetes deaths, age-specific, crude and age-standardized diabetes mortality rates (both for diabetes as the underlying cause of death and for diabetes as one of the causes) according to nationality

	Age group	*Belgian origin*			*North African origin*		
		n[a]	*Diabetes mortality rates (95% CI)*		*n*[a]	*Diabetes mortality rates (95% CI)*	
Diabetes mortality (Diabetes as the underlying cause of death)	45–49	3		17.8 (0.0–38.0)	0		0.0 (0.0–0.0)
	50–54	3		16.9 (0.0–36.0)	0		0.0 (0.0–0.0)
	55–59	3		19.0 (0.0–40.4)	1		64.6 (0.0–191.3)
	60–64	2		14.2 (0.0–33.8)	3		209.4 (0.0–446.0)
	65–69	3		19.1 (0.0–40.6)	3		288.7 (0.0–615.0)
	70–74	18		99.6 (53.6–145.5)	1		200.0 (0.0–591.6)
	Total (45–74)	32	Crude	32.5 (21.3–43.8)	8	Crude	80.7 (34.8–159.0)
			ASMR[b]	32.5 (21.3–43.8)		ASMR[b]	123.4 (26.1–220.8)
Diabetes-related mortality (Diabetes as one of the causes)	45–49	6		35.6 (7.1–64.1)	1		29.6 (0.0–87.7)
	50–54	9		50.7 (17.6–83.8)	0		0.0 (0.0–0.0)
	55–59	10		63.2 (24.0–102.3)	3		193.9 (0.0–413.2)
	60–64	20		141.5 (79.5–203.5)	12		837.4 (365.6–1309.2)
	65–69	42		266.8 (186.2–347.4)	5		481.2 (60.4–902.0)
	70–74	94		519.9 (415.1–624.7)	5		1000.0 (127.9–1872.1)
	Total (45–74)	181	Crude	184.0 (157.3–210.8)	26	Crude	262.2 (171.3–384.2)
			ASMR[b]	184.0 (157.3–210.8)		ASMR[b]	417.4 (227.2–607.7)

[a]*n,* number of diabetes deaths.

[b]ASMRs, directly standardized to the 45- to 74-year-old female Belgian population of the BCR.

As for the relationship between *parity* and diabetes-related mortality, particularly high diabetes-related mortality is observed among *grandmultiparous* women. Adjusting the analyses for educational attainment attenuates the relationship between grandmultiparity and diabetes-related mortality to some extent, suggesting that selection contributes to the association. Causal mechanisms may furthermore play an important part. Several physiological and biosocial pathways can be thought of, including: permanent alterations in glucose and lipid metabolism due to successive pregnancies,[14] weight accumulation from one pregnancy to another,[22] chronic stress,[23,24] gestational diabetes[25] (although studies on the association between high parity and gestational diabetes have produced conflicting results)[26] etc. In this study, *childless* women do not have an increased risk of dying from diabetes, as opposed to other studies. This latter research often attributes the observed excess diabetes mortality among nulliparous women to selection effects, e.g. hormonal changes associated with insulin resistance are related to both diabetes and infertility.[8] A possible explanation for the fact that nulliparous women in our cohort do not have higher diabetes-related mortality may be childlessness by choice. Possibly, the nulliparous group is no longer largely composed of insulin-resistant women or women with health problems, but consists of both women who choose to remain childless and women who are not capable of childbirth.

Our results indicate that *age at first birth* is strongly associated with diabetes-related mortality. Women who were *teenage mothers* are at particularly high risk of dying from diabetes. Mechanisms underlying this association encompass both selection effects and causal influences. Adjusting for educational attainment, the association between early motherhood and diabetes-related mortality attenuates. One possible explanation is that childhood disadvantage is associated with both diabetes-related mortality and educational difficulties (selection effect). However, the relationship may also be the other way around: early motherhood may lead to a disruption of educational careers. Moreover, obesity may play an important part in the relationship between age at first birth and diabetes-related mortality. Previous research[27] has shown an increased obesity risk among Belgian girls of immigrant origin as well as among socially disadvantaged girls from early adolescence on. As these groups also have a high prevalence of adolescent pregnancies, the increased diabetes-related mortality among teenage mothers may be (partly) due to differences in obesity (selection effect). However, obesity may also be an intermediating factor as

Table 3 Age-adjusted diabetes-related MRRs and 95% CIs for parity and age at first birth

	Number of diabetes deaths and age-adjusted diabetes-related MRRs							
	Model 1[a] *(all women)*[b]		*Model 2*[a] *(parous women)*[b]		*Model 3*[a] *(parous women)*[b]		*Model 4*[a] *(parous women)*[b]	
	n[c]	*MRRs (95% CI)*	*n*[c]	*MRRs (95% CI)*	*n*[c]	*MRRs (95% CI)*	*n*[c]	*MRRs (95% CI)*
Parity								
0	20	0.88 (0.51–1.51)				(Excluded)		(Excluded)
1	46	1.18 (0.77–1.81)			46	1.22 (0.79–1.88)	46	1.09 (0.71–1.70)
2 (ref.)	38	1.00			38	1.00	38	1.00
3	29	1.47 (0.90–2.38)			29	1.40 (0.86–2.27)	29	1.42 (0.88–2.31)
4–8	45	2.40 (1.56–3.70)			45	1.98 (1.27–3.07)	45	1.83 (1.17–2.88)
≥9	7	4.60 (2.05–10.30)			7	2.80 (1.21–6.47)	7	2.27 (0.95–5.46)
Age at first birth								
<18			20	7.48 (4.20–13.34)	20	5.65 (3.07–10.40)	20	3.67 (1.96–6.89)
18–25			101	2.01 (1.32–3.05)	101	1.87 (1.22–2.85)	101	1.50 (0.98–2.31)
25–30 (ref.)			28	1.00	28	1.00	28	1.00
30–35			12	1.38 (0.70–2.71)	12	1.45 (0.73–2.86)	12	1.44 (0.73–2.85)
≥35			3	1.04 (0.32–3.42)	3	1.09 (0.33–3.62)	3	1.10 (0.33–3.66)

[a]Variables included in the different models are: Model 1: age and parity/Model 2: age and age at first birth/Model 3: age, parity and age at first birth/ Model 4: age, parity, age at first birth and education.

[b]All women: $n = 98\,231$/parous women: $n = 82\,057$.

[c]*n*, Number of diabetes deaths.

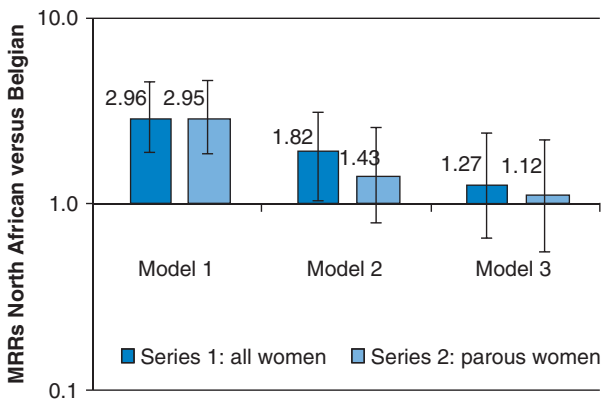

Fig. 1 Age-adjusted diabetes-related MRRs and 95% CIs for North African versus Belgian origin. *Series 1* (all women, $n = 98\,231$): Model 1 includes age and ethnic origin. Model 2 is adjusted for age and parity and Model 3 for age, parity and education. *Series 2* (parous women, $n = 82\,057$): Model 1 includes age and ethnic origin. Model 2 is adjusted for age, parity and age at first birth and Model 3 for age, parity, age at first birth and education.

teenage pregnancies are characterized by higher weight gain compared with adult pregnancies.[28] There are indications that this higher—excessive—gestational weight gain not only contributes to adolescent obesity,[29] but also increases the risk of becoming overweight during adulthood.[22,30]

Particularly, high diabetes-related mortality is found among North African women. This excess burden is largely accounted for by the reproductive factors age at first birth and parity. To establish which mechanisms underlie these associations, further research is needed. Yet, as parity and age at first birth explain a substantial part of the excess diabetes-related mortality among North African women, pregnancy might provide an excellent opportunity for early diabetes prevention, such as promoting a healthy lifestyle. Given the strong 'education–diabetes-related mortality' association, public health policies addressing diabetes might furthermore benefit from grappling with social disparities in: access to and quality of care, health behaviour, diabetes knowledge, health perceptions etc. Improving the educational profile of the population as a whole and of some (nationality) groups in particular may be a less obvious but nonetheless successful way of reducing the diabetes burden.

What is already known on this topic

Previous research has already established a relationship between parity and diabetes mortality. Moreover, excess diabetes-related mortality among North African women echoes findings from prior studies on diabetes prevalence

and mortality, showing a high diabetes (mortality) burden among North African women in Europe.[1,3]

What this study adds

To our knowledge, this is the first study to explore the association between age at first birth and diabetes-related mortality. An important finding of our research is that teenage motherhood is a risk factor for diabetes-related mortality. This investigation also adds to our understanding of variations in diabetes-related mortality by nationality group among women. The excess diabetes-related mortality among North African women largely disappears when the reproductive factors age at first birth and parity are taken into account. So, accounting for women's fertility history may shed new light on differences in diabetes-related mortality by nationality among women.

Limitations of this study

The limitations of this study are largely related to the study design. As this is a retrospective cohort study linking census data to vital records, analyses are strongly dependent on the quality and amount of information reported in census and death/emigration records, e.g. lifestyle variables such as obesity are not included in the 2001 census, shutting the door on estimating the effect of these variables on the observed associations. On the other hand, the census is a unique and rich database, providing high-quality information on, for example, parity and socioeconomic position. A number of diabetes mortality registration issues are furthermore of account. First, as more than 50% of the death certificates reporting diabetes have ICD-code E14 (unspecified diabetes), it is not feasible to distinguish between type 1 and type 2 diabetes. In practice, however, the results are unlikely to be affected in a significant way, since ~85–90% of all persons with diabetes have type 2 diabetes. Second, diabetes is rarely registered as the underlying cause of death, as it is often not the 'immediate' cause of the decease. Taking into account diabetes-related mortality therefore gives a more accurate estimation of the diabetes burden. Third, to the extent that reporting of diabetes on death certificates differs according to nationality group, cross-nationality comparisons of diabetes-related mortality may be difficult to establish. Yet, the fact that the results of this study mirror findings from previous diabetes morbidity studies suggests that the observed variations in diabetes-related mortality are not solely the outcome of differential registration practices, but reflect real differences in the burden of diabetes.

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