DOI: 10.1111/1471-0528.12253
www.bjog.org

Association between gestational diabetes mellitus and subsequent overactive bladder among premenopausal female twins

G Tettamanti,[a] AN Iliadou,[a] NL Pedersen,[a] R Bellocco,[a,b] D Altman[a,c]

[a] Division of Obstetrics and Gynaecology, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden [b] Department of Statistics and Quantitative Methods, University of Milano-Bicocca, Milan, Italy [c] Department of Clinical Science, Danderyd Hospital, Karolinska Institutet, Stockholm, Sweden
Correspondence: Mr G Tettamanti, Department of Medical Epidemiology and Biostatistics, 171 77 Karolinska Institutet, Stockholm, Sweden. Email giorgio.tettamanti@ki.se

Accepted 8 March 2013. Published Online 7 May 2013.

Objective To investigate the association between a history of gestational diabetes mellitus (GDM) and overactive bladder (OAB) in women of premenopausal age.

Design Population-based study.

Setting The Swedish Twin Register.

Population In 2005, a total of 14 094 female twins born between 1959 and 1985 in the Swedish Twin Registry participated in a comprehensive survey on common exposures and complex diseases. Structured questions provided information on GDM and OAB. The present study was designed as a cross-sectional analysis including all women in the cohort having given birth before 2005 (n = 7855).

Methods A logistic regression model based on generalised estimating equations was used to derive odds ratios (ORs).

Main outcome measure The association between a history of GDM and OAB was estimated using ORs with 95% confidence intervals (CIs).

Results The prevalence of OAB in women with a history of GDM was 19.1% compared with 10.7% in women without GDM. This corresponded to a two-fold increased odds of OAB in women with a history of gestational diabetes (OR 2.13, 95% CI 1.48–3.05). After adjusting the analysis for age, body mass index, parity, smoking, and diabetes mellitus, having had GDM was associated with doubled odds of OAB (OR 1.88, 95% CI 1.26–2.80).

Conclusions A history of GDM was positively associated with OAB among women of premenopausal age. The association does not seem to be mediated by body mass index or type-I or type-II diabetes mellitus.

Keywords Diabetes, gestational diabetes, overactive bladder.

Please cite this paper as: Tettamanti G, Iliadou A, Pedersen N, Bellocco R, Altman D. Association between gestational diabetes mellitus and subsequent overactive bladder among premenopausal female twins. BJOG 2013;120:1289–1295.

Introduction

Overactive bladder (OAB) is a highly prevalent symptom syndrome, defined as 'urinary urgency, with or without urgency incontinence, usually with frequency and nocturia' by the International Continence Society (ICS).[1] In a cross-sectional survey of community-dwelling adults in five industrialised countries, the overall prevalence of OAB was nearly 12%.[2] It has been estimated that OAB affects approximately 33 million people in the USA,[3] and is associated with a considerable impact on all aspects of quality of life.[4]

Observational studies suggest that OAB is over-represented among women with type–I and type–II diabetes mellitus.[5–9] Although the underlying mechanisms are not fully understood, several theories by which diabetes may cause OAB in women have been proposed. Peripheral neuropathy, microvascular complications, decreased production of nerve growth factor in the bladder, and changes of nitric oxide regulation in the uroepithelium, subsequent to hyperglycaemia, are some of the suggested pathways linking the two conditions.[10,11] Previous studies are mostly performed in postmenopausal women, and very little is known about the contribution of gestational diabetes mellitus

(GDM) to OAB in women of reproductive age. Results from cross-sectional and prospective studies have suggested that GDM might be associated with an increased risk of urinary incontinence.[12,13] In this large population-based study we investigated the association between a history of GDM and OAB in a female population of premenopausal age.

Methods

Data sources

The Swedish Twin Registry, established in the late 1950s, contains data on nearly all twins born in Sweden since 1886.[14] In 2005 data for the present study were derived from a comprehensive survey on common complex diseases and common exposures among all twins in the Swedish Twin Registry born between 1959 and 1985 (n = 42 852; described in detail previously).[15,16] The overall response rate to the survey, the Study of Twin Adults: Genes and Environment (STAGE), was 66% among the women (n = 14 094), and the present study included all women that had given birth (n = 7855).

In this study we used both self-reported information and national registry data to ascertain which women had diabetes mellitus and a history of GDM. The Inpatient Register, established in 1964, and with complete national coverage since 1987, contains virtually complete information on hospitalization, and has been described in detail previously.[17] The Medical Birth Register has recorded data for all deliveries in Sweden since 1973, and includes information on maternal, obstetrical, and neonatal outcomes. The registers also include the individually unique national registration number that is assigned to all Swedish residents, thereby allowing unambiguous record linkage. The study was approved by the Regional Research Ethics Board at Karolinska Institutet, and conforms with the STROBE guidelines for reporting observational studies (www.strobe-statement.org).

Data ascertainment

The entire questionnaire contained approximately 1300 questions divided into 34 sections using a branching format, meaning that participants were asked follow-up questions only if they responded positively to key initial questions.[15] Overactive bladder was defined according to the International Continence Society criteria as a positive response to either of the following the questions: 'Do you experience sudden urgency to void with little or no warning?' or 'Do you have involuntary loss of urine in connection with sudden and strong urgency to void?' The self-reported history of GDM was classified as: number of occasions, treatment, and whether or not women developed diabetes mellitus after pregnancy. Diabetes mellitus (types I or type II) was recorded as present or not at the time of the survey. Information on relevant covariates, including body mass index (BMI), parity, smoking, educational level, and age, was derived from the survey.

Additional information about diabetes mellitus and GDM was obtained from the nationwide Inpatient Register and the Medical Birth Register using the International Classification of Disease (ICD) codes: for GDM, 648W (ICD-9) and O24.4–O24.5 (ICD-10); for diabetes mellitus, 250 (ICD-8), 250 (ICD-9), and E10–E11 and O24.0–O24.3 (ICD-10).

Statistics

In order to evaluate the association between a history of GDM and OAB, a logistic regression model was applied using generalised estimating equations in order to adjust for the dependency within twin pairs. GDM was characterised as a dichotomous exposure (ever or never) for case ascertainment.

The logistic regression model was first adjusted for established risk factors for lower urinary tract dysfunction, including age (categorised into four groups, based on quartile distribution), parity (one child or more than one child), and BMI (categorised into four categories according to World Health Organization guidelines).[18] Thereafter, we adjusted the analysis for smoking (never, former smoker, or current smoker), educational level (elementary, high school, or college/university degree), and the occurrence of diabetes mellitus (yes or no). We additionally included interaction terms between GDM and diabetes mellitus, and between GDM and BMI, to test whether the effect of GDM differed among women with and without diabetes (and among women with low and high BMIs). Odds ratios (ORs) were estimated with 95% confidence intervals (95% CIs). All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, NC, USA).

Results

A total of 7855 women from the STAGE survey were eligible for analysis, of which 863 women had OAB (11%) and 200 women had a history of GDM (2.5%). Using the registers we identified an additional four women with a diagnosis of diabetes mellitus and 25 women with a diagnosis of GDM: therefore, a total of 225 women (2.9%) in this study had a history of GDM. The mean age was 37.6 years (standard deviation, SD, 5.7 years) for the entire cohort and 38.0 years (SD 6.0 years) for women with OAB.

Table 1 presents the characteristics for all women in the study and for those with OAB. Women with OAB had a higher prevalence of both gestational diabetes (5.0 versus 2.6%, crude OR 2.13, 95% CI 1.49–3.05) and diabetes mellitus (2.6 versus 1.5%, crude OR 2.11, 95% CI 1.29–3.48), compared with women without OAB. Among women with

OAB, being overweight or obese, having a lower level of education, and being a current smoker was more common than among women without OAB.

Characteristics of women with gestational diabetes are shown in Table 2. Among women with a history of GDM, 43/225 (19.1%) reported OAB. In women with both conditions (GDM and OAB), current smoking was nearly twice as common as compared with women affected only by GDM (41.9 versus 19.8%): this corresponded to a crude OR of 3.82 (95% CI 1.65–8.83). In this subgroup of women, obesity was also positively associated with OAB. Other comparisons between women with GDM and women with both GDM and OAB were statistically non-significant.

Table 3 shows the results from logistic regression modelling. After adjusting the analysis for age, BMI, and parity, having had GDM still doubled the odds of OAB (OR 2.11, 95% CI 1.47–3.03). Further adjustment for smoking and educational level had only a minor effect on the point estimates for the association between GDM and OAB (OR 2.13, 95% CI 1.48–3.05). In the final model we also adjusted for diabetes mellitus in order to estimate the effect of GDM on OAB that is not mediated by diabetes mellitus. The association between a history of GDM and OAB remained statistically significant (OR 1.88, 95% CI 1.26–2.8), but the significant association with diabetes mellitus was lost (OR 1.42, 95% CI 0.83–2.43). We tested the possible interaction between GDM and diabetes mellitus, and between GDM and BMI, but neither of these interactions were found to be statistically significant.

Table 1. Characteristics of the women who had given birth in the STAGE study

	Women without overactive bladder *n* = 6992	Women with overactive bladder *n* = 863	Crude OR (95% CI)
Gestational diabetes mellitus			
Yes	182 (2.6)	43 (5.0)	2.13 (1.49–3.05)
No	6125 (87.6)	734 (85.0)	1.0 (reference)
Missing	685 (9.8)	86 (10.0)	–
Diabetes mellitus			
Yes	104 (1.5)	22 (2.6)	2.11 (1.29–3.48)
No	7592 (96.6)	840 (97.3)	1.0 (reference)
Missing	136 (1.9)	1 (0.1)	–
Age			
19–26 years	296 (4.2)	37 (4.2)	1.16 (0.78–1.73)
27–33 years	1446 (20.7)	171 (19.8)	1.0 (reference)
34–40 years	2727 (39.0)	304 (35.2)	0.95 (0.77–1.16)
41–47 years	2523 (36.1)	351 (40.7)	1.19 (0.98–1.46)
BMI category			
<18.5	137 (2.0)	19 (2.2)	1.09 (0.65–1.84)
18.5–24.9	4.564 (65.3)	537 (62.2)	1.0 (reference)
25.0–29.9	1293 (18.5)	193 (22.4)	1.34 (1.12–1.61)
>30.0	384 (5.5)	98 (11.4)	2.41 (1.87–3.10)
Missing	614 (8.8)	16 (1.8)	–
Parity			
1	1787 (25.6)	251 (29.1)	1.0 (reference)
>1	5205 (74.4)	612 (70.9)	0.82 (0.7–0.96)
Smoking			
No	3776 (54.0)	453 (52.5)	1.0 (reference)
Former	1732 (24.8)	207 (24.0)	1.07 (0.89–1.27)
Current	1465 (20.9)	198 (22.9)	1.24 (1.03–1.49)
Missing	19 (0.3)	5 (0.6)	–
Educational level			
Low	431 (6.2)	71 (8.2)	1.37 (1.03–1.82)
Medium	3.788 (54.2)	466 (54.0)	1.0 (reference)
High	2763 (39.5)	326 (37.8)	0.88 (0.75–1.03)
Missing	10 (0.1)	–	–

Values are number of women (%).

Table 2. Characteristics of women with a history of gestational diabetes mellitus

	Women with gestational diabetes mellitus but without overactive bladder *n* = 182	Women with gestational diabetes mellitus and overactive bladder *n* = 43	Crude OR
Occurrence of gestational diabetes mellitus			
Once	118 (64.8)	33 (76.7)	1.0 (reference)
More than once	41 (22.5)	6 (13.9)	0.56 (0.21–1.48)
Do not know	23 (12.6)	4 (9.3)	–
Diabetes mellitus			
Yes	60 (33.0)	24 (55.8)	1.94 (0.94–3.91)
No	121 (66.5)	19 (44.2)	1.0 (reference)
Missing	1 (0.4)	–	–
Age			
19–26 years	7 (3.8)	3 (7.0)	1.8 (0.29–11.2)
27–33 years	17 (9.3)	5 (11.6)	1.0 (reference)
34–40 years	72 (39.6)	15 (34.9)	0.72 (0.22–2.37)
41–47 years	86 (47.2)	20 (46.5)	0.75 (0.23–2.39)
Missing –		–	–
BMI category			
<18.5	4 (2.2)	1 (2.3)	1.04 (0.11–9.74)
18.5–24.9	109 (59.9)	22 (51.2)	1.0 (reference)
25.0–29.9	33 (18.1)	11 (25.6)	1.9 (0.81–4.45)
>30	15 (8.2)	7 (16.3)	4.84 (1.48–15.8)
Missing	21 (11.5)	2 (4.6)	–
Parity			
1	29 (15.9)	12 (27.9)	1.0 (reference)
>1	153 (84.1)	31 (72.1)	0.36 (0.16–0.84)
Missing –		–	–
Smoking			
No	88 (48.3)	16 (37.2)	1.0 (reference)
Former	57 (31.3)	9 (20.9)	1.03 (0.42–2.53)
Current	36 (19.8)	18 (41.9)	3.82 (1.65–8.83)
Missing	1 (0.4)	–	–
Educational level			
Low	11 (6.0)	6 (13.9)	2.43 (0.74–7.99)
Medium	97 (53.3)	23 (53.5)	1.0 (reference)
High	73 (40.1)	14 (32.6)	0.69 (0.32–1.46)
Missing	1 (0.4)	–	–

Values are number of women (%).

Discussion

Main findings

In the present study, a history of GDM was positively associated with OAB among women of premenopausal age. The results were robust after adjusting the analysis for diabetes mellitus, BMI, and other confounding factors, which had little or no impact on the association. This indicates that the effect of gestational diabetes on OAB is not simply mediated by BMI or by diabetes mellitus later in life. One in five women with a history of GDM reported OAB with or without urinary incontinence, which is almost double the reported prevalence rates of the general population in industrialised countries.[2]

Interpretation

An overall prevalence of OAB of 19% makes it significantly more common than other commonly reported diabetes-related complications, such as retinopathy and neuropathy, in women with manifest type-II diabetes mellitus.[19] Given that the female population in our study was mostly of premenopausal age, the high prevalence of OAB among women with a history of GDM is noteworthy.

Gestational diabetes mellitus often debuts during the second trimester as a result of physiological changes in glucose metabolism and a gradual increase in insulin resistance, and is considered an established risk factor for type-II diabetes mellitus later in life.[20] We suggest that the association between GDM and OAB could be a result of subclinical

Table 3. Odds ratios for overactive bladder in multivariable logistic regression analysis

	Adjusted OR*	Adjusted OR**	Adjusted OR***
No GDM or no DM	1.0 (reference)	1.0 (reference)	1.0 (reference)
Gestational diabetes mellitus	2.11 (1.47–3.03)	2.13 (1.48–3.05)	1.88 (1.26–2.80)
Diabetes mellitus	2.03 (1.23–3.34)	2.02 (1.23–3.33)	1.42 (0.83–2.43)

*Adjusted for age, body mass index, and parity.
**Adjusted for age, body mass index, parity, smoking, and educational level.
***Adjusted for age, body mass index, parity, smoking, and educational level. Gestational diabetes mellitus (GDM) and diabetes mellitus (DM) are included in the same model.

cystopathy in the aftermath of pregnancy. This process may share pathoetiological mechanisms with diabetes mellitus, and includes neurogenic, myogenic, and microvascular bladder sequela of chronic hyperglycaemia in individuals who may not have developed diabetes. A subclinical (not diagnosed) progression towards diabetes in women with latent type-II diabetes mellitus would also explain why diabetes is not positively associated with OAB in our analysis, despite there being evidence of an association between the two, for example from the longitudinal Nurses' Health Study, which suggested that the development of type–II diabetes mellitus may especially affect urgency urinary incontinence.[21]

The prevalence of lower urinary tract dysfunction, including OAB, increases significantly during pregnancy.[22,23] Adverse effects of GDM on bladder morphology may add to the burden of pregnancy-induced stress on the bladder, including hormonal changes, hyperaemia, and urinary frequency. Thus, GDM could be viewed upon as a stress test for the lower urinary tract with regard to the liability of developing OAB later in life, and may be an important risk factor for OAB even in women who do not develop diabetes later in life. Attempts to determine which diabetes-related risk factors have the greatest influence on lower urinary tract dysfunction have so far not been able to identify any single prognostic factor to explain the association. Diabetes duration, type, and treatment, HbA1c levels, and fasting glucose did not show any relation to type of bladder dysfunction or severity in a study assessing the relationship between diabetes-specific risk factors and urinary incontinence.[24] Previous studies have reported that diabetes mellitus,[5–9] GDM,[12,13] and metabolic syndrome[25] are positively associated with urinary incontinence, suggesting that metabolic effects of pregnancy may explain some of the urinary symptoms observed after the delivery. Efforts to optimise glycaemic control and to prevent or delay the progression to manifest type–II diabetes mellitus has obvious general health benefits, and may delay the onset of diabetes complications, including urologic complications.[9,10]

Strengths and limitations

We have reported novel information on an often-disregarded area of female diabetes care, and our study has several strengths. In this nationwide study we focused on women of reproductive age, where ageing has not diluted the effect of obstetrical factors such as GDM on urinary symptoms.[26] Moreover, we used a large-scale, population-based design, the classification of the primary outcome conforms to international standards, and we had access to information on important risk factors and confounding factors, including BMI and the occurrence of postpartum diabetes mellitus. A previous cross-sectional study reported that stress urinary incontinence is common among women with a history of GDM[12]; however, in this study there was no control group without GDM, and a recent prospective study on the association between GDM and urinary incontinence was not able to adjust for postpartum diabetes mellitus or postpartum body weight.[13]

Among the limitations of our study we recognise that the cross-sectional study design does not allow a more detailed analysis of the temporal aspects of the association. As a consequence, it is possible that women had OAB symptoms before the diagnosis of gestational diabetes. Furthermore, unmeasured factors related to pregnancy and delivery, such as macrosomia, may to some extent influence the positive association between GDM and OAB. Another limitation of this study is that there were insufficient numbers of twin pairs discordant for both the outcome and the exposure. Therefore, we could not determine whether the association between OAB and GDM was confounded by familial factors, such as common genes or shared environmental factors. Even though twins are generally smaller at birth and have a shorter gestational age compared with singletons, a recent study has shown that twins do not differ in mortality and morbidity compared with their singleton siblings in general.[27] GDM is a heterogeneous condition ranging in severity from those with only mild insulin resistance, where dietary restrictions are sufficient for glucose control, to those who

will need large doses of insulin. In the present study there were insufficient numbers of women with a history of GDM to allow for a more detailed analysis on how severity of GDM influenced the association. We therefore cannot rule out the possibility that among women with a more severe type of GDM the odds of OAB have been underestimated.

Conclusion

In the present study we found a positive association between a history of GDM and OAB, which does not seem to be mediated by diabetes mellitus or BMI later in life. As GDM is to some extent a preventable condition,[28] the fact that GDM could be associated with a higher risk of postpartum OAB provides further rationale for the active prevention and management of GDM. Longitudinal studies that control for postpartum diabetes mellitus and postpartum BMI are needed to confirm these findings.

Disclosure of interests

DA is a consultant for Gynecare Scandinavia, Ethicon US, and Contura A/S. GT, NLP, RB, and ANI declare that they have no conflicts of interest.

Contribution to authorship

GT conceived and designed the experiments, analysed the data, and drafted the article. DA conceived and designed the experiments, participated in the writing of the article, and provided funding. NLP conceived and designed the experiments, participated in the writing of the article and provided funding. RB conceived and designed the experiments, analysed the data, and participated in the writing of the article and analysis. ANI conceived and designed the experiments, and participated in the writing of the article.

Details of ethics approval

The study was approved by the Regional Ethics Board at Karolinska Institutet (approval reference number 2007/538-31/4).

Funding

The study was supported by grants from the National Institute of Digestive Disorders and Kidney Diseases (U01 DK066134 to NLP), the Swedish Research Council (K2010-21574-01–4 to DA), and the OAB-LUTS Competitive Grants Program, Pfizer Inc. (to DA).

Acknowledgement

This study was based on data from the Swedish Twin Register. ■

References

1 Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn* 2002;21:167–78.
2 Irwin DE, Milsom I, Hunskaar S, Reilly K, Kopp Z, Herschorn S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. *Eur Urol* 2006;50:1306–14; discussion 14-5.
3 Cardozo L, Coyne KS, Versi E. Validation of the urgency perception scale. *BJU Int* 2005;95:591–6.
4 Chiaffarino F, Parazzini F, Lavezzari M, Giambanco V. Gruppo Interdisciplinare di Studio Incontinenza U. Impact of urinary incontinence and overactive bladder on quality of life. *Eur Urol* 2003;43:535–8.
5 Ebbesen MH, Hannestad YS, Midthjell K, Hunskaar S. Diabetes and urinary incontinence - prevalence data from Norway. *Acta Obstet Gynecol Scand* 2007;4:1–7.
6 Jackson SL, Scholes D, Boyko EJ, Abraham L, Fihn SD. Urinary incontinence and diabetes in postmenopausal women. *Diabetes Care* 2005;28:1730–8.
7 Lawrence JM, Lukacz ES, Liu IL, Nager CW, Luber KM. Pelvic floor disorders, diabetes, and obesity in women: findings from the Kaiser Permanente Continence Associated Risk Epidemiology Study. *Diabetes Care* 2007;30:2536–41.
8 Lifford KL, Curhan GC, Hu FB, Barbieri RL, Grodstein F. Type 2 diabetes mellitus and risk of developing urinary incontinence. *J Am Geriatr Soc* 2005;53:1851–7.
9 Brown JS, Vittinghoff E, Lin F, Nyberg LM, Kusek JW, Kanaya AM. Prevalence and risk factors for urinary incontinence in women with type 2 diabetes and impaired fasting glucose: findings from the National Health and Nutrition Examination Survey (NHANES) 2001–2002. *Diabetes Care* 2006;29:1307–12.
10 Brown JS, Wessells H, Chancellor MB, Howards SS, Stamm WE, Stapleton AE, et al. Urologic complications of diabetes. *Diabetes Care* 2005;28:177–85.
11 Hill SR, Fayyad AM, Jones GR. Diabetes mellitus and female lower urinary tract symptoms: a review. *Neurourol Urodyn* 2008;27:362–7.
12 Kim C, McEwen LN, Sarma AV, Piette JD, Herman WH. Stress urinary incontinence in women with a history of gestational diabetes mellitus. *J Womens Health* 2008;17:783–92.
13 Chuang CM, Lin IF, Horng HC, Hsiao YH, Shyu IL, Chou P. The impact of gestational diabetes mellitus on postpartum urinary incontinence: a longitudinal cohort study on singleton pregnancies. *BJOG* 2012;119:1334–43.
14 Lichtenstein P, De Faire U, Floderus B, Svartengren M, Svedberg P, Pedersen NL. The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies. *J Intern Med* 2002;252:184–205.
15 Lichtenstein P, Sullivan PF, Cnattingius S, Gatz M, Johansson S, Carlstrom E, et al. The Swedish Twin Registry in the third millennium: an update. *Twin Res Hum Genet* 2006;9:875–82.
16 Tettamanti G, Altman D, Pedersen NL, Bellocco R, Milsom I, Iliadou AN. Effects of coffee and tea consumption on urinary incontinence in female twins. *BJOG* 2011;118:806–13.
17 Ludvigsson JF, Andersson E, Ekbom A, Feychting M, Kim JL, Reuterwall C, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011;11:450.
18 Ezzati M. *Comparative Quantification of Health Risks Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*. Geneva: World Health Organization; 2004.

19 Phelan S, Kanaya AM, Subak LL, Hogan PE, Espeland MA, Wing RR, et al. Prevalence and risk factors for urinary incontinence in overweight and obese diabetic women: action for health in diabetes (look ahead) study. *Diabetes Care* 2009;32:1391–7.

20 Djelmis J, Desoye G, Ivanisevic M. *Diabetology of Pregnancy. Frontiers in Diabetes*. Vol 17, Basel: Karger; 2005.

21 Danforth KN, Townsend MK, Curhan GC, Resnick NM, Grodstein F. Type 2 diabetes mellitus and risk of stress, urge and mixed urinary incontinence. *J Urol* 2009;181:193–7.

22 Van BH, Bruinse HW, Van de Pole G, Heintz AP, Van der Vaart CH. What is the effect of overactive bladder symptoms on woman's quality of life during and after first pregnancy? *BJU Int* 2006;97:296–300.

23 Wesnes SL, Rortveit G, Bo K, Hunskaar S. Urinary incontinence during pregnancy. *Obstet Gynecol* 2007;109:922–8.

24 Ebbesen MH, Hannestad YS, Midthjell K, Hunskaar S. Diabetes related risk factors did not explain the increased risk for urinary incontinence among women with diabetes. The Norwegian HUNT/EPINCONT study. *BMC Urol* 2009;9:11.

25 Kim YH, Kim JJ, Kim SM, Choi Y, Jeon MJ. Association between metabolic syndrome and pelvic floor dysfunction in middle-aged to older Korean women. *Am J Obstet Gynecol* 2011;205:71 e1–8.

26 Fritel X, Ringa V, Quiboeuf E, Fauconnier A. Female urinary incontinence, from pregnancy to menopause: a review of epidemiological and pathophysiological findings. *Acta Obstet Gynecol Scand* 2012;91:901–10.

27 Oberg S, Cnattingius S, Sandin S, Lichtenstein P, Morley R, Iliadou AN. Twinship influence on morbidity and mortality across the lifespan. *Int J Epidemiol* 2012;41:1002–9.

28 Han S, Middleton P, Crowther CA. Exercise for pregnant women for preventing gestational diabetes mellitus. *Cochrane Database Syst Rev* 2012;7:CD009021.

