Int J Clin Exp Pathol 2015;8(7):8512-8515
www.ijcep.com /ISSN:1936-2625/IJCEP0007467

*Original Article*

# Factors associated with diabetes mellitus prediction among pregnant Arab subjects with gestational diabetes

Naji Aljohani[1,2,3*], Amal Al Serehi[4], Amjad M Ahmed[5], Badr Aldin M Buhary[2], Saad Alzahrani[1,2], Eeman At-Taras[6], Najla Almujally[1], Maha Alsharqi[1], Mohammed Alqahtani[7], Mussa Almalki[1,2]

*[1]Faculty of Medicine, King Saud bin Abdul-Aziz University for Health Sciences, Riyadh 22490, Saudi Arabia; [2]Specialized Diabetes and Endocrine Center, King Fahd Medical, Riyadh 59046, Saudi Arabia; [3]Prince Mutable Chair for Biomarkers of Osteoporosis, College of Science, King Saud University, Riyadh 11451, Saudi Arabia; [4]Department of Maternal-Fetal Medicine, King Fahd Medical, Riyadh 59046, Saudi Arabia; [5]Women's Specialized Hospital, Riyadh, King Fahd Medical, Riyadh 59046, Saudi Arabia; [6]College of Sciences and Health Professions, King Saud Bin Abdul-Aziz University for Health Sciences, Riyadh 22490, Saudi Arabia; [7]Department of Medicine, King Abdul Aziz Medical, Riyadh 11426, Saudi Arabia*

Received March 1, 2015; Accepted June 22, 2015; Epub July 1, 2015; Published July 15, 2015

**Abstract:** There is scarcity of available information on the possible significant risk factors related to diabetes mellitus (DM) prediction among expectant Saudi mothers with gestational diabetes mellitus (GDM). The present study is the first to identify such risk factors in the Arab cohort. A total of 300 pregnant subjects (mean age 33.45 ± 6.5 years) were randomly selected from all the deliveries registered at the Obstetrics Department of King Fahad Medical City, Riyadh Saudi Arabia from April 2011 to March 2013. Demographic and baseline glycemic information were collected. A total of 7 highly significant and independent risk factors were identified: age, obesity, and family history of DM, GDM < 20 weeks, macrosomia, insulin therapy and recurrent GDM. Among these factors, subjects who had insulin therapy use are 5 times more likely to develop DMT2 (*p*-value $3.94 \times 10^{-14}$) followed by recurrent GDM [odds-ratio 4.69 (Confidence Interval 2.34-4.84); $P = 1.24 \times 10^{-13}$). The identification of the risk factors mentioned with their respective predictive powers in the detection of DMT2 needs to be taken seriously in the post-partum assessment of Saudi pregnant patients at highest risk.

**Keywords:** GDM, Saudi, pregnancy, diabetes mellitus

## Introduction

Gestational diabetes mellitus (GDM) is a common pregnancy-associated complication defined as "any degree of glucose intolerance with onset or first recognition during pregnancy" [1, 2]. It has been reported recently that an increase in the prevalence of GDM has been reported in several ethnic groups in the past 20 years, and this increase grossly reflects the incidence of diabetes mellitus type 2 (DMT2) in the concerned population [3]. The role of ethnicity as an independent predictor on the progression of GDM to DMT2 aside from conventional risk factors such as advanced maternal age, obesity and family history of DM is consistently confirmed in several studies, with non-European women, Asian women in particular, having a higher predisposition than other groups [4, 5]. Granted that there has been a considerable amount of literature on GDM done in the Arab world, Saudi Arabia in particular, remains understudied as compared to other developed nations with respect to maternal hyperglycemia progressing to full blown DMT2. Previous studies done in Saudi Arabia were able to identify unique risk factors for GDM such as multi-parity and presence of periodontal disease [6, 7]. In this single center cross-sectional study, we aimed to determine the risk factors for DMT2 among randomly selected pregnant subjects with GDM.

## Methodology

Subjects were taken from a database of all deliveries that took place from April 2011 to

**Table 1.** Demographics and Characteristics of Subjects

| Parameter | |
|---|---|
| N | 300 |
| Saudi Nationality | 283 (94.7) |
| Family History of DM | 215 (71.9) |
| GDM Duration (more than 20 weeks) | 216 (72.0) |
| History of Macrosomia | 62 (20.7) |
| Insulin Therapy | 85 (28.4) |
| Recurrent GDM | 112 (37.3) |
| Age (years) | 33.45 ± 6.5 |
| Pre-pregnancy weight (kg) | 73.8 ± 18.4 |
| OGTT (0-hour) (mmol/l) | 5.5 ± 1.3 |
| OGTT (2-hour) (mmol/l) | 7.7 ± 3.1 |
| HbA1c | 5.9 ± 0.9 |
| Post-partum weight (kg) | 76.2 ± 18.7 |

Note: Data presented as percentage (%) for frequencies; mean ± standard deviation for continuous variables.

March 2013 at the Obstetrics Department of King Fahad Medical City, Riyadh, Saudi Arabia. Out of the total 1700 deliveries, 400 were randomly selected using the RAND function of MS Excel 2010. Information gathered include demographics such as nationality, family history of GDM, date of GDM diagnosis (if any), history of macrosomia, insulin therapy and recurrent GDM. Clinical data include age, pre-pregnancy weight (kg), oral glucose tolerance test results, HBA1c and post-partum weight (kg). Exclusion criteria include subjects with other co-morbidities aside from DMT2 such as thyroid, heart, kidney, liver and infectious diseases. Those with incomplete information were also taken out, bringing the final total sample size to N = 300. The study has been approved by the Institutional Review Board of King Fahad Medical City Research Center, Riyadh, Saudi Arabia.

*Data analysis*

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 16.5 (Chicago IL, USA). Frequencies were presented as percentages and continuous variables were presented as mean ± standard deviation. Analysis of variance (ANOVA) was used to compare groups. Multiple logistic regression analysis was used to determine risk using DMT2 as dependent variable and age, obesity, family history of DMT2, GDM less than 20 weeks, macrosomia, insulin therapy and recurrent GDM as independent variables. Significance set at $P < 0.05$.

## Results

**Table 1** shows the clinical characteristics of all subjects. Almost all of the expectant mothers who participated in the present study were Saudis (94.7%). More than 70% of the subjects had a family history of DM, 37.3% had a previous history of GDM, 28.4% were on insulin therapy and more than 20% had a history of macrosomia. The rest of the characteristics are shown in **Table 1**.

Next we compared the subjects based on the presence of IFG and DMT2 (**Table 2**). Subjects with DMT2 had the highest prevalence of family history of DM (93.2%) and the lowest prevalence of GDM beyond 20 weeks (20.5%) than both normal and IFG groups. In addition, half of the DMT2 group had a history of macrosomia with an overwhelming majority (84.1%) on insulin therapy, and these were statistically significant as compared to normal and IFG groups. In the normal group and as expected, the mean age was significantly younger than both the DMT2 and IFG group. The normal group also had the lowest pre-pregnancy weight, BMI, HBA1c and post-partum weight as compared to both group. The rest of the comparisons are shown in **Table 2**.

**Table 3** shows the odds-ratios for DMT2 using the different risk factors identified. Subjects on insulin therapy and those who had GDM less than 20 weeks had the highest risk for DMT2, with the presence of either factor translating to 5 times more likely to harbor DMT2 independent of other factors [OR 4.94 (3.27-7.75), $P = 3.94 \times 10^{-14}$; OR 4.69 (3.12-7.06), $P = 1.24 \times 10^{-13}$, respectively]. Furthermore, patients who had recurrent GDM are 3.37 times more likely to have DMT2 ($P = 6.56 \times 10^{-11}$). Other independent significant risk factors identified include age, obesity, family history of DMT2 and macrosomia (**Table 3**).

## Discussion

The present cross-sectional study provides first-hand additional information on the capacity of several risk factors to detect who among pregnant Saudi women are at highest risk for

**Table 2.** Characteristics of Subjects According to Glucose Tolerance

| Parameters | Normal | IFG | T2DM |
|---|---|---|---|
| N | 158 | 98 | 44 |
| Saudi Nationality | 94.9 | 93.9 | 93.2 |
| Family History of DM | 63.9 | 75.3 | 93.2* |
| GDM Duration (more than 20 weeks) | 87.3 | 70.4 | 20.5*,! |
| History of Macrosomia | 11.4 | 22.4 | 50.0*,! |
| Insulin Therapy | 13.3 | 27.8 | 84.1*,! |
| Recurrent GDM (≥ 2 times) | 7.0 | 18.4 | 18.2 |
| Age (years) | 32.17 ± 6.91 | 34.50 ± 6.03* | 35.70 ± 5.33* |
| Pre-pregnancy weight (kg) | 68.67 ± 16.7 | 76.90 ± 18.56* | 85.18 ± 17.33! |
| Body Mass Index (kg/m$^2$) | 28.17 ± 6.37 | 30.95 ± 7.14* | 33.62 ± 5.97*,! |
| OGTT (0-hour) (mmol/l) | 4.86 ± 0.37 | 5.51 ± 0.64* | 7.88 ± 1.61*,! |
| OGTT (2-hour) (mmol/l) | 5.84 ± 1.08 | 7.96 ± 1.69* | 13.61 ± 3.06*,! |
| HbA1c | 5.51 ± 0.44 | 5.88 ± 0.64* | 7.04 ± 1.42*,! |
| Post-partum weight (kg) | 70.78 ± 16.26 | 80.12 ± 18.64* | 87.21 ± 20.34* |

Note: Data presented as percentage (%) for frequencies; mean ± standard deviation for continuous variables; *denotes significance as compared to normal; !denotes significance as compared to IFG; significant at $P < 0.01$.

**Table 3.** Odds Ratio for DMT2 using several variables of interest as dependent variables

| Risk Factor | Odds-Ratio | 95% Confidence Interval | *P*-Value |
|---|---|---|---|
| Age > 35 years | 1.87 | 1.31-2.49 | $3.36 \times 10^{-4}$ |
| Obesity (> 30 kg/m$^2$) | 2.40 | 1.70-3.38 | $6.29 \times 10^{-7}$ |
| Family History of DMT2 | 2.21 | 1.46-3.34 | 0.00017 |
| GDM less than 20 weeks | 4.69 | 3.12-7.06 | $1.24 \times 10^{-13}$ |
| Macrosomia | 2.75 | 1.87-4.05 | $3.04 \times 10^{-7}$ |
| Insulin Therapy | 4.94 | 3.27-7.75 | $3.94 \times 10^{-14}$ |
| Recurrent GDM | 3.37 | 2.34-4.84 | $6.56 \times 10^{-11}$ |

Note: *P*-value significant at $P < 0.01$.

DMT2 progression. In the results, expectant mothers with DMT2 had the highest pre-pregnancy weight and BMI, confirming a very recent study that having a high pre-pregnancy BMI is an independent predictor for both early and late DMT2 converters after GDM [8]. Other conventional significant risk factors for GDM such as advancing age and family history of DM were also observed to be consistent in predicting DMT2 in the present study.

Other highly significant risk factors in the progression to DMT2 among Saudi expectant mothers are the use of insulin therapy and GDM recurrence. Insulin treatment has also been one of the major risk factors for post-partum diabetes in a Turkish population [9]. The use of insulin per se in the treatment of hyperglycemia is an indication of poor β-cell function. It has been observed that patients who formerly had gestational diabetes also had a marked decrease in insulin sensitivity and a modest decline in β-cell function, and these changes are significantly associated with diabetes onset [10]. It is worthy to note that insulin therapy is commonly used among pregnant patients with diabetes mellitus type 1 (DMT1), is frequently needed to optimize glycemic control among pregnant patients with DMT2 and less common among those with GDM [11]. Recurrent GDM on the other hand, while significantly associated with DMT2 among Saudi pregnant patients, has not been associated thus far in the deterioration of glucose metabolism and cardiovascular risk, at least in European women [12].

The authors acknowledge some limitations. The cross-sectional nature of the present study cannot determine whether the outcome (DMT2) followed exposure (risk factors) in time or vice versa. This needs to be confirmed using a longitudinal design. Furthermore while the sample size was enough to elicit extremely significant *p*-values, the findings cannot be generalized since it is a single-center study. Nevertheless, the identification of highly significant risk fac-

tors, specifically insulin use and recurrent GDM to predict DMT2 among randomly selected Saudi pregnant women is the first documentation in this cohort, and carries both scientific merit and clinical significance in the assessment and management of this population postpartum, particularly in this part of the world. Further studies involving neonatal outcomes and other variables not included such as socioeconomic factors, diet and physical activity should be done to determine these factors also affect DMT2 progression.

## Acknowledgements

The authors would like to thank King Fahd Medical City Research Center for funding and approving the study. The authors are also grateful to Carla Suguitanm, Noron Sybil and Marife de Vera for their assistance.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Naji Aljohani, Faculty of Medicine, King Saud Bin Abdulaziz University for Health Sciences, PO Box 59046, Riyadh 11525, Saudi Arabia. Tel: 0096612889999 Ext. 7185; Fax: 0096612889999 Ext. 6717; E-mail: najijohani@gmail.com

## References

[1] Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiler JL, Lowe LP, McIntyre HD, Oats JJ, Omori Y, Schmidt MI. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010; 33: 676-82.

[2] American Diabetes Association. Diagnosis and classification of diabetes mellitus (Position Statement). Diabetes Care 2009; 32 Suppl 1: S62-S67.

[3] Ferrara A. Increasing prevalence of gestational diabetes mellitus: a public health perspective. Diabetes Care 2007; 30 Suppl 2: S141-6.

[4] Ignell C, Shaat N, Ekelund M, Berntorp K. The impact of ethnicity on glucose homeostasis after gestational diabetes mellitus. Acta Diabetol 2013; 50: 927-34.

[5] Kousta E, Efstathiadou Z, Lawrence NJ, Jeffs JA, Godsland IF, Barrett SC, Dore CJ, Penny A, Anyaoku V, Millauer BA, Cela E, Robinson S, McCarthy MI, Johnston DG. The impact of ethnicity on glucose regulation and the metabolic syndrome following gestational diabetes mellitus. Diabetologia 2006; 4991: 36-40.

[6] Al-Rowaily MA, Abolfotouh MA. Predictors of gestational diabetes mellitus in a high-parity community in Saudi Arabia. East Mediterr Health J 2010; 16: 636-41.

[7] Habib FA. Evaluation of periodontal status among Saudi females with gestational diabetes and its relation to glucose and lipid homeostasis in Ohud Hospital, Al Madina Al-Munwarrah. Int J Health Sci (Qassim) 2009; 3: 143-54.

[8] Kwak SH, Choi SH, Jung HS, Cho YM, Lim S, Cho NH, Kim SY, Park KS, Jang HC. Clinical and genetic risk factors for type 2 diabetes at early or late port partum after gestational diabetes mellitus. J Clin Endocrinol Metab 2013; 98: E744-52.

[9] Tura A, Grassi A, Winhofer Y, Guolo A, Pacini G, Mari A, Kautzky-Willer A. Progression to type 2 diabetes in women with former gestational diabetes: time trajectories of metabolic parameters. PLoS One 2012; 7: e50419.

[10] McElduff A, Moses RG. Insulin therapy in pregnancy. Endocrinol Metab Clin North Am 2012; 41: 161-73.

[11] Winhofer Y, Tura A, Prikoszovich T, Winzer C, Schneider B, Pacini G, Luger A, Kautzky-Willer A. The impact of recurrent gestational diabetets on maternal metabolic and cardiovascular risk factors. Eur J Clin Invest 2013; 43: 190-7.

[12] Akinci B, Celtik A, Genc S, Yener S, Demir T, Secil M, Kebapcilar L, Yesil S. Evaluation of postpartum carbohydrate intolerance and cardiovascular risk factors in women with gestational diabetes. Hynecol Endocrinol 2011; 27: 361-7.