

Risk factors of gestational diabetes mellitus in the refugee population in Gaza Strip: a case-control study

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عوامل اختطار الإصابة بالسكري أثناء فترة الحمل في السكان اللاجئين بقطاع غزة: دراسة حالة ذات شواهد عريفه الكسيح، نيك محمد زكي، يوسف الجيش، لين كنج سون

الخلاصة: أُجريت دراسة حالة استيعادية ذات شواهد في الفترة من آذار/ مارس وحتى حزيران/ يونيو 2011 برعاية وكالة الأمم المتحدة لإغاثة وتشغيل اللاجئين الفلسطينيين في الشرق الأدنى (الأونروا) من أجل تحديد عوامل اختطار الإصابة بالسكري أثناء فترة الحمل في أوساط السكان اللاجئين بقطاع غزة. وُجمعت البيانات الخاصة بالخصائص الاجتماعية والديموغرافية للأمهات ومعدل انتشار السكري أثناء فترة الحمل المُشخص وفق المعايير التي وضعتها منظمة الصحة العالمية وذلك من العيادات التابعة لوكالة الأونروا التي جرى فيها تشخيص النساء الفلسطينيات بالسكري أثناء فترة الحمل أثناء الأحمال السابقة، مع اعتبار النساء غير المصابات بالسكري أثناء فترة الحمل كشواهد. واستُخدمت الخصائص الاجتماعية والديموغرافية، ومنسب كتلة الجسم في الفترة السابقة على الحمل، وتاريخ التوليد، وتاريخ الأسرة كمتغيرات الدراسة. وتم التعرف على إجمالي 189 حالة من حالات السكري أثناء فترة الحمل. وكانت عوامل الاختطار الأكثر أهمية لحدوث السكري أثناء فترة الحمل هي: وجود تاريخ للإجهاض أكثر من مرة؛ وزيادة الوزن قبل الحمل؛ ووجود تاريخ لوفيات الأجنة؛ ووجود تاريخ للولادات القيصرية؛ ووجود تاريخ إيجابي في الأسرة للإصابة بالسكري. ويواصل معدل حدوث السكري أثناء فترة الحمل المُشخص الارتفاع في أوساط السكان اللاجئين بقطاع غزة. وينبغي إعطاء الأولوية داخل الوكالات المعنية بالصحة العمومية المحلية لرفع الوعي بالنتائج الضائرة للسكري أثناء فترة الحمل على صحة الأمهات وحديثي الولادة في أوساط السكان اللاجئين بقطاع غزة.

ABSTRACT To determine the risk factors of gestational diabetes mellitus in refugee populations in the Gaza Strip, a retrospective case-control study was performed between March and June 2011 in the United Nations Relief and Works Agency (UNRWA) primary health care clinics. Data were collected on maternal sociodemographics and the prevalence of diagnosed GDM according to World Health Organization criteria from clinics where postnatal Palestinian refugee women had been diagnosed with GDM during previous pregnancies, and non-GDM women were used as controls. Sociodemographic characteristics, pre-pregnancy body-mass index (BMI), obstetrics history and family history of diabetes were used as study variables. In total, 189 incident cases of GDM were identified. The most significant risk factors for GDM were: history of miscarriage more than once; overweight before pregnancy; history of stillbirth; history of caesarean birth; and positive family history of diabetes mellitus.

Facteurs de risque de diabète gestationnel chez les réfugiées de la Bande de Gaza : étude cas-témoin

RÉSUMÉ Afin d'identifier les facteurs de risque de diabète gestationnel chez les réfugiées de la Bande de Gaza, une étude cas-témoin rétrospective a été menée entre mars et juin 2011 dans les dispensaires de soins de santé primaires de l'Office de secours et de travaux des Nations Unies pour les réfugiés de Palestine dans le Proche-Orient (UNRWA). Des données sur les caractéristiques socioéconomiques des mères et la prévalence du diabète gestationnel (diagnostiqué d'après les critères de l'Organisation mondiale de la Santé) ont été recueillies auprès des dispensaires de l'UNRWA où, après leur accouchement, des réfugiées palestiniennes avaient reçu un diagnostic de diabète gestationnel dans leurs grossesses passées. Un groupe témoin était constitué de femmes non diabétiques. Les variables d'étude étaient les caractéristiques sociodémographiques, l'indice de masse corporelle (IMC) prégestationnel, les antécédents obstétricaux et les antécédents familiaux de diabète. Au total, 189 cas incidents de diabète gestationnel ont été identifiés. Les facteurs de risque les plus importants étaient les suivants : antécédents d'au moins deux fausses couches ; surpoids avant la grossesse ; antécédent de mortinaissance ; antécédent de césarienne ; et antécédents familiaux positifs de diabète sucré.

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Introduction

Gestational diabetes mellitus (GDM), which is defined as glucose intolerance with the onset or first detection during pregnancy, is said to complicate approximately 1%–16% of all pregnancies with an increased risk of perinatal morbidity and mortality and an increased risk of developing diabetes in the future [1,2]. Previous studies have indicated that south Asian and Arab ethnicities have high prevalence rates of GDM related to parity, body mass index (BMI) and maternal age [3,4]. Gestational diabetes is a condition that can be effectively controlled, thereby decreasing the associated risks and eventually leading to the delivery of healthy infants. Conversely, the consequences of risk factors in women may predispose them to developing GDM during pregnancy. These predisposition factors include: increased maternal age, high body weight, high parity, previous birth of large baby and family history of diabetes mellitus [5]. According to the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study, a large-scale multinational epidemiological study, the risk of adverse maternal, fetal and neonatal outcomes continuously increases as a function of maternal glycaemia at 24–28 weeks of gestation [6]. There was no cause for most of these complications, except preventing and early recognition of GDM as a major health concern. Because the prevalence of GDM is increasing in parallel to the ongoing epidemic of obesity and type 2 diabetes in reproductive age women [7], understanding the significance of risk factors becomes a public health concern. According to the Palestinian Health Report of 2007, the total population of the Gaza Strip was 1 337 230 of whom 70% were refugees [8]. The average percentage of women of childbearing age was 22.4%, while total fertility rate in the Gaza Strip was 5.4%, one of highest rates in the region.

Pregnancy, which was once acknowledged as a natural process, is considered to be associated with real or potential threats to the comfort and well-being of pregnant women and their families [8]. In a war-torn place such as the Gaza Strip, evidence with regard to the association between these factors and GDM is scarce. No previous publications on this subject matter for this type of subject population are currently available [9]. Identification of GDM risk factors will provide information to strengthen public health measures and help to prevent maternal, fetal and neonatal development of overt diabetes and cardiovascular complications. In this context, a retrospective case–control study was conducted to elucidate risk factors of GDM in the refugee population in the Gaza Strip.

The primary objective of this study was to determine the risk factors of GDM in the refugee population in the Gaza Strip.

Methods

This was a retrospective case–control study carried out at United Nations Relief and Works Agency (UNRWA) clinics in the Gaza Strip. UNRWA for Palestine Refugees is one of the largest United Nations programmes, serving a population of 4 760 000 Palestine refugees worldwide under its mandate in 2010. The Agency's mission is to assist Palestine refugees in achieving their full potential in human development until a durable and just solution is found for the refugee issue [10]. This study was approved by the Human Research Ethics Committee (HREC) of Universiti Sains Malaysia (USM) and UNRWA in the Gaza Strip. In this study, obstetrical records of GDM patients who delivered in 2010 were retrieved from the annual statistics at UNRWA clinics and reviewed. Participants were drawn from refugee women attending the UNRWA postnatal clinics in the Gaza

Strip. Data collection ran from March 2011 to June 2011 in UNRWA clinics. Women aged 18 and above with a GDM history based on the gestational diabetes clinic files at UNRWA were consecutively recruited. All pregnant women attending the UNRWA clinics were routinely subjected to an oral glucose tolerance test (OGTT) at 24–28 weeks or 32–34 weeks gestation for some cases with impaired glucose tolerance. The diagnosis of GDM was based upon the results of both the fasting sample and/or the two-hour OGTT test. Women with abnormal results were then referred to a specialized GDM clinic.

WHO recommends simultaneous screening and diagnosis using a 75 g oral glucose tolerance test. Based on the WHO criteria, screening for all pregnant women was conducted at 24–28 weeks by using fasting glucose test after an 8–14 hour fast followed by a 75 g oral glucose tolerance test (OGTT). WHO guidelines classify pregnant women as having diabetes with fasting venous plasma glucose ≥ 7.0 mmol/L and 2-hour post-glucose load level ≥ 11.1 mmol/L [11].

In this study, 189 postnatal GDM women who met the inclusion criteria (women aged 18 years and above, no history of medical diseases, had already been diagnosed with GDM in their previous pregnancy according to WHO criteria and delivered in 2010) were recruited. For control, 189 postnatal women without pre-gestational type 1 or 2 diabetes and any chronic diseases were matched with age and place of residency were recruited.

All participants were informed and gave written consent. For some illiterate populations, the sample was guided by the researcher in person during the survey. After oral and/or written consent from the participants, the researcher conducted the survey at the UNRWA postnatal clinics. We established the following exclusion criteria: women with pre-gestational

type 1 or 2 diabetes and severe chronic diseases.

The risk factors that were assessed included sociodemographic characteristics of height, age, weight, place of residency, number of previous pregnancies and caesarean section, stillbirth, family history of diabetes, past and current obstetrics history and educational level. Height and weight was observed and recorded. Weight prior to pregnancy was taken verbally from the participants and confirmed from weight recorded in the first prenatal visit in early pregnancy (before eight weeks gestation); and for women who were not sure about their weight before pregnancy we relied on weight in first antenatal visit, and in follow-up visits. Weights and heights were noted for the visits in early pregnancy in order to calculate the pre-pregnancy BMI (kg/m^2). For an alpha error of 5% and a power of 80%, assuming the prevalence of gestational diabetes in the Gaza Strip was less than 10% and a value of 0.5 as an estimate of the population proportion, using the power and sample size calculation, the minimum sample size was estimated to be 166 each of case and control sample size.

A well designed and pilot-tested questionnaire was used to collect data. Face-to-face interviews were conducted by qualified nurses using a validated self-administered questionnaire in Arabic. The questionnaire covered the sociodemographic characteristics of the pregnant women, family, current and past obstetrics history, medical history and type of maternal complications. The survey instrument was then tested on 30 randomly selected pregnant women from the list at the UNRWA clinics for the validity of the questionnaire. Some corrections and modifications were made after considering the discrepancies that had been found during the pilot study.

For achieving good face validity, the questionnaire was reviewed by experts from the obstetrics and gynaecology researchers at Universiti Sains Malaysia.

Further statistical validity of the questionnaire was assessed by Pearson test to determine the validity of the questionnaire structure as well as testing the validity of each section within the whole survey questionnaire. The correlation coefficients are considered significant at $\alpha < 0.05$.

The rates of selected potential risk factors were calculated for women with and without GDM. Chi-squared tests were performed to test statistical significance. To assess the independent effect of each individual risk factor attributed to GDM, multiple logistic regressions were applied. The adjusted odds ratio (OR) and the 95% confidence interval (CI) were derived from the coefficient of the logistic model and its standard error. All statistical analyses were performed using SPSS version 20. Significance was assumed if the *P*-value was less than 0.05.

Results

According to the WHO criteria, GDM was diagnosed in 189 women with gestational diabetes in their most recent pregnancy in 2010. These participants with GDM were included as a case group and were compared with the 189 without GDM as control group. Table 1 shows that the difference between the mean age and standard deviation (SD) (34.1, SD 6.56) among the women diagnosed with GDM and the control group (34.2, SD 6.77) was not statistically significant ($P = 0.859$). The women diagnosed with GDM had a similar mean and SD (162.4 cm, SD 5.42) height in comparison to the control group (162.3, SD 5.39) with no significant association ($P = 0.924$). However, the results showed the mean and SD of weight (81.1 kg, SD 13.16) in women diagnosed with GDM was higher than the mean and SD (69.0, SD 14.15) in the control group with significant association as $P < 0.001$. We found that GDM was twice as high in illiterate

women (13.8%) when compared to the control group (6.3%). The findings of the present study revealed that there was no significant difference between women with GDM and the control group regarding place of residency.

Table 2 shows the correlated GDM risk factors using univariate analysis. Results show that women overweight before pregnancy with increased BMI had 1.07 and 1.15 times greater risk of developing GDM. Furthermore, women with lower levels of education, an increased number of pregnancies (more than four), and history of previous miscarriages (more than once), a history of stillbirth, a history of a large baby, and a positive family history of diabetes mellitus had 2.47, 5.92, 5.98, 6.92, 5.52 and 28.83 times the odds of developing GDM respectively. However, the result did not show any significant correlation between the place of residency, advanced maternal age and parity, and developing GDM.

Place of residency, height, maternal age, educational level, gravidity, parity, history of large baby and BMI were excluded from the final model as these factors were considered as confounders. Hence, the final multivariate logistic analysis revealed that women with a history of abortion more than once [aOR 4.93, 95% CI: 2.20–11.04], a history of stillbirth [aOR 3.35, 95% CI: 1.21–9.23], and a positive family history of diabetes mellitus [aOR 17.60, 95% CI: 4.84–64.01] had higher ORs in comparison to others risk factors. However, women overweight before pregnancy [aOR 1.07, 95% CI: 1.04–1.09], and with history of caesarean birth [aOR 2.92, 95% CI: 1.54–5.53], had lower ORs for developing GDM (Table 3).

Discussion

Gestational diabetes mellitus is a long-known condition. Controversies still surround the standardized risk factors for this condition all over the world [12].

Table 1 Sociodemographic characteristic of women with gestational diabetes mellitus (GDM) and the control group (n = 378)

Variable	GDM (n = 189) Mean (SD)	Controls (n = 189) Mean (SD)	Mean difference (95% CI)	t statistic	P-value
Age (years)	34.1 (6.56)	34.2 (6.77)	0.122 (-1.22 to 1.47)	0.177	0.859
Height (cm)	162.4 (5.42)	162.3 (5.39)	0.052 (1.14 to 1.04)	-0.095	0.924
Weight (kg)	81.1 (13.16)	69.0 (14.15)	-12.08 (-14.85 to 9.32)	-8.59	<0.0001
	No. (%)	No. (%)		χ² statistic	
Residency					
North zone	61 (32.3)	60 (31.7)		2.51	0.473
Gaza City	40 (21.2)	40 (21.2)			
Middle zone	50 (26.5)	40 (21.2)			
South zone	38 (20.1)	49 (25.9)			
Level of education					
Illiterate	26 (13.8)	12 (6.3)		15.78	0.001
Preparatory	50 (26.5)	29 (15.4)			
Secondary	63 (33.2)	77 (40.5)			
Graduate	50 (26.5)	71 (37.5)			

SD = standard deviation; CI = confidence interval.

This study attempted to identify the most significant risk factors for GDM in the Gaza Strip. Several risk factors for GDM have been previously identified. The most common recognized factors are advanced maternal age and maternal body-mass index ≥ 25 [13]. This study did not show any correlation between age, height and place of residency as predisposing to developing GDM. However, the findings of the present study revealed that there is association between women's weight and level of education as a predisposition to developing GDM.

Few studies have examined the correlation between level of education and prevalence of GDM. Bo et al. (2002) in a case-control study in Turin, Italy, reported that lower levels of education are associated with an increased risk of GDM [14]. Similarly, recent studies declared the relationship between metabolic disorder in women and lower educational level [15–17].

Our results in the univariate analysis confirmed that most related risk factors for GDM were a history of miscarriage more than once, being overweight before pregnancy, a

greater BMI, level of education, history of stillbirth, history of large baby, history of caesarian birth and positive family history of diabetes mellitus. Several previous articles have reported that advanced maternal age, history of stillbirth and history of previous diagnosed GDM are globally considered as classical and traditional risk factors [6,18,19]. However, the present study found no significant association between maternal age and developing GDM. Interestingly, this result was consistent with that of United Kingdom National Institute for Health and Clinical Excellence Guidelines recommendation, which excluded the maternal age of pregnant women as a risk factor for GDM screening [20]. In agreement with a study in Kuwait, our results found that GDM is mostly associated with a young age group, and mainly among those with a positive family history of diabetes mellitus [21]. This means that even young women can be at high risk for GDM. Our study also agreed with previous reports indicating obesity, history of caesarean birth and positive family history of diabetes mellitus as

significant risk factors for developing GDM [6,21,22].

The present study showed that history of miscarriage more than once, being overweight before pregnancy, history of stillbirth, history of caesarean birth and positive family history of diabetes mellitus were strongly correlated with developing GDM. This finding was consistent with a study in Tehran that reported GDM is highly associated in women with positive family history of diabetes mellitus, pre-pregnancy obesity and history of miscarriage [23]. Our study revealed a significant association of GDM with history of stillbirth. It has been reported that such complications are associated with GDM [24,25]. That is to say, gestational diabetes with its vascular complications is a significant risk factor for stillbirth and perinatal death. Similar findings have been reported in Syed et al.'s review regarding perinatal mortality [24].

We found a significant correlation between developing GDM and pre-pregnancy weight. This finding is in agreement with a recent systematic review, including 20 articles related to

Table 2 Risk factors for gestational diabetes mellitus (GDM): univariate logistic regression model

Variable	Regression coefficient(B)	Unadjusted OR (95% CI)	Wald statistic	P-value
Place of residency				
North zone	0	1		
Gaza City	0.017	1.01 (0.52–1.78)	0.03	0.954
Middle zone	–0.207	0.81 (0.47–1.40)	0.54	0.460
South zone	0.271	1.31 (0.75–2.28)	0.91	0.338
Height	0.002	1.00 (0.96–1.04)	0.09	0.924
Weight before pregnancy	0.070	1.07 (1.05–1.09)	53.59	< 0.0001
Body mass index	0.141	1.15 (1.10–1.20)	36.77	< 0.0001
Maternal age (years)				
< 30	0	1		
30–35	–0.446	0.64 (0.41–0.99)	3.89	0.048
> 35	0.333	1.39 (0.48–4.02)	0.38	0.537
Education level				
Illiterate	1.58	4.90 (0.97–24.58)	3.73	0.053
Preparatory	0.907	2.47 (1.45–4.22)	11.05	0.001
Secondary	0.136	1.14 (0.07–1.87)	0.29	0.589
Graduated	0	1		
Gravidity				
< 2	0	1		
2–4	0.648	1.9 (0.59–6.10)	1.19	0.274
> 4	1.779	5.92 (1.88–18.63)	9.25	0.002
Parity				
< 2	0	1		
2–4	–0.728	0.48 (0.22–1.01)	3.65	0.056
> 4	0.174	1.19 (0.56–2.49)	0.21	0.646
History of abortion				
None	0	1		
Once	1.39	4.02 (2.33–6.91)	25.27	< 0.0001
More than once	1.78	5.98 (3.16–11.30)	30.36	< 0.0001
History of still birth				
No	0	1		
Yes	1.93	6.92 (2.01–23.83)	9.43	0.002
History of large baby				
No	0	1	30.25	< 0.0001
Yes	1.71	5.52 (3.0–10.16)		
Family history of diabetes mellitus				
No	0	1		
Yes	3.36	28.83 (8.85–93.94)	31.12	< 0.0001

OR = odds ratio; CI = confidence interval.

obesity, and maternal outcomes published from 1980 to 2006. Eight out of these 20 studies were conducted in the US; the other 12 were conducted in Canada, Australia, Italy, France, United Arab Emirates, Finland and

the UK [26]. The review declared that the risk of having GDM is about twofold, fourfold and eightfold higher among overweight, obese and severely obese reproductive-aged women, respectively, when compared with

normal-weight reproductive-aged women.

Our present study did not show a significant correlation between an increase in parity and an increase in the number of pregnancies with GDM.

Table 3 Risk factors for gestational diabetes mellitus: multivariable logistic regression model

Variable	Regression coefficient (B)	Adjusted OR (95% CI)	Wald statistic
History of abortion			
None	0	1	
Once	1.13	3.11 (1.55– 6.21)	10.30**
More than once	1.59	4.93 (2.20– 11.04)	15.06**
Weight before pregnancy	0.06	1.07 (1.04–1.09)	29.31**
History of still birth: yes	1.20	3.35 (1.21–9.23)	5.46*
History of caesarean delivery: yes	1.07	2.92 (1.54–5.53)	10.93**
Family history of diabetes mellitus: yes	2.86	17.60 (4.84–64.01)	21.76**

*P-value < 0.05; **P-value < 0.01.

OR = odds ratio; CI = confidence interval.

However, controversy still exists regarding multiparity and pregnancy as risk factors for GDM [27]. Until recently, only a few studies reported an increase in gravidity and parity as significant risk factors for GDM [12,23,28]. Major et al. (1998) have justified the recurrence rate of gestational diabetes mellitus among women with short pregnancy intervals, as those women are more susceptible to GDM recurrence because their bodies have not been granted adequate time to revert to pre-pregnancy status [28].

Moreover, our findings showed that women with history of miscarriages (more than once) were at higher risk for developing GDM. A similar study in India has found that the prevalence of GDM progressively increased in women with one, two or more previous miscarriages by 3.1%, 8.2% and 11.9%, respectively [12]. On the same lines, another study in China has shown a strong association between a history of miscarriage and impaired glucose tolerance in pregnancy (Yang et al. 2009) [29]. Although previous studies and this study have found similar significant associations, there is no biological evidence which correlates the development of GDM and miscarriage. This possible correlation requires further investigation.

Conclusion

In conclusion, WHO criteria for screening for GDM remain a good instrument to identify GDM in refugee populations in war-torn countries (like the Gaza Strip). Because the increase in GDM is a public health concern, it is critical to know the risk factors associated with developing GDM, not only to become more aware of this alarming increasing trend in GDM, but also to provide baseline information about the determinants of GDM, which could help incorporate early intervention measures for refugee women in the Gaza Strip and elsewhere.

Some limitations have to be addressed in the present study. First, it was a relatively small sample size among refugees, which might not allow the results to be generalized to the greater population. From the findings of this study, and considering its limitations, we conclude that according to WHO criteria GDM continues to prevail in the Gaza Strip. We recommend that the UNRWA health authorities in the Gaza Strip strengthen maternal health programmes and postpartum prevention policies to change these trends in GDM and to prevent chronic diabetes mellitus in GDM patients and their offspring.

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