Diabetes incidence and influencing factors in women with and without gestational diabetes mellitus: A 15 year population-based follow-up cohort study

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ABSTRACT

Aim: Very few extensive follow-up investigations evaluating patients with history of gestational diabetes mellitus (GDM) have been documented. We conducted this longitudinal study to estimate the incidence of diabetes and its predictors in women with and without GDM.

Method: A total of 2458 eligible women, aged 20–50 years (476 with GDM and 1982 without GDM) were selected from among participants of the Tehran Lipid and Glucose study, based on the World Health Organization definition for GDM screening. Pooled logistic regression was used to assess the association between time-dependent covariates and diabetes.

Results: The incidence rate of diagnosed diabetes was 9/1000 for women with GDM and 4/1000 for their counterparts, without GDM. Kaplan-Meier curve indicated a significantly shorter median time for developing diabetes in women with a history of GDM (6.95 years [IQ: 4.22–10.71]), compared to their healthy peers (8.45 years [IQ: 5.08–10.89]). BMI and previous family history of diabetes were found as major risk factors for future diabetes in women with GDM.

Conclusion: The results presented here lead to better identification and selection of at-risk women with prior GDM history.

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1. Introduction

Type 2 diabetes mellitus (T2DM), as a chronic metabolic disease, is a major epidemiologic global concern which necessitates the early detection of risk factors and identification of at- risk populations [1]. Women with the history of gestational diabetes mellitus (GDM) are one of these challenging high-risk groups [2]. GDM, occurring in about 7% of all pregnancies and a well-established risk factor for T2DM [3], alters glucose tolerance and metabolism as well as insulin resistance [4]. In fact, when the elevated insulin secretion cannot meet the needs of pregnancy-induced insulin resistance status, GDM develops [5]. In a recent systematic review using 24 relevant papers, the prevalence of GDM among Iranian women was reported 3.41% (varying between 1.3% and 18.6%) [6].

Depending on the ethnicity of the study population, follow-up period and the diagnostic criteria used, approximately, up to 60% of women with GDM may progress to T2DM [7]. Data available suggest that GDM significantly increases both the adverse short-term pregnancy outcomes such as hypertensive disorders, macrosomia and caesarian section rate [8] as well as, the likelihood of long-term metabolic conditions in both mother and offspring [9]. Reports confirm the elevated risk of cardiovascular disease [10] and decreased pancreatic beta cell function [11] in women with previous GDM. Therefore, pregnancies affected by diabetes need to be followed and monitored regularly, in order to plan and intervene efficiently to prevent any adverse metabolic outcome.

We have previously shown that during a 9-year follow-up, T2DM was diagnosed in 27.3% of women with GDM and its cumulative incidence was about 3-fold higher than in normal women [12]. In the current study we aimed to investigate the incidence of T2DM in women with GDM compared to non-GDM women and to find out the influencing factors in diabetes progression, using data from a 15-year follow-up study of Tehran Lipid and Glucose Study (TLGS).

2. Subjects

The current study is a 15-year-follow up of women whose index pregnancy was diagnosed with GDM; study subjects were recruited from the Tehran Lipid and Glucose Study (TLGS) [13], a long term prospective general population study initiated in 1998 to determine the prevalence and risk factors of non-communicable diseases. In this study 15,005 people, aged ≥3, were invited to participate. The participants undergo a follow-up visit every 3 years and demographic, anthropometric, reproductive and metabolic features and general physical examinations as well as laboratory measurements are recorded. Until now TLGS has completed five follow-up phases at 3-year intervals (phase 1: 1999–2001, phase 2: 2002–2005, phase 3: 2005–2008, phase 4: 2008–2011 and phase 5: 2011–2014). Current data are available for five phases, including baseline and four follow-ups.

A total of 4076 women, aged 20–50 years with at least one term pregnancy at the beginning of the study met the eligibility criteria; excluded women were those with overt diabetes (n = 270), impaired fasting glucose (IFG) (n = 240), impaired glucose tolerance (IGT) (n = 296) and simultaneous IGT and

IFG (n = 137) at baseline. Of 3133 remained participants, 485 (16.5%) women were present only at baseline visit and had no follow-up data and were hence considered as lost to follow-up. Also, 190 women had missing data and were removed from analysis.

Of the remaining 2458 women, 476 had history of GDM and 1982 were without GDM; of these 39(8.2%), 64(13.4%), 146 (30.7%) and 227(47.7%) in the GDM group and 233(11.8%), 305 (15.4%), 577(29.1%) and 867(43.7%) in the non-GDM group were present at just one, two, three and four follow-up visits, respectively. In other words, 437 (91.8%) of the subjects with GDM had at least two follow-up visits. Similarly, 1749 (88.2%) of the participants in the non-GDM group had at least two follow-up visits. Also, 1444 (72.9%) and 373 (78.4%) of the subjects had at least three follow-up visits in non-GDM and GDM groups, respectively.

All the patients were present at the baseline of the study and had at least one follow-up visit, otherwise they were considered as cases lost to follow-up (Fig. 1).

The study proposal was approved by the Medical Ethics Committee of the Research Institute for Endocrine Sciences and written informed consent was obtained from all participants.

3. Materials and methods

Subjects were interviewed using pretested questionnaires and during clinical examinations anthropometric measurements were assessed by trained examiners at each follow-up. Details of examinations and procedures have been previously published [12,14]. In brief, weight was measured with minimum clothing to the nearest 100 g. Height was measured with a tape measure in a standing position, with shoulders in normal alignment. Waist circumference (WC) was measured midway at the level of umbilicus between the lower rib margin and the iliac-crest at the end of a gentle expiration. Hip circumference (HC) was measured with measuring tape to the nearest 0.1 cm, following which waist to hip ratio (WHR) was calculated. Body mass index (BMI) was calculated by dividing weight (kg) by height (m^2).

Fasting blood sugar was tested after 12–14 h of fasting. Plasma glucose was measured using enzymatic colorimetric method by glucose oxidase kit (Pars Azmoon, Tehran, Iran) with inter- and intra- assay variation coefficients of <2.2%. All laboratory evaluations were performed at the TLGS research center.

For GDM screening, the World Health Organization (WHO) criteria were used [15]. In our country, GDM screening is a national program conducted as a part of routine prenatal care. To ascertain GDM, for women with negative history of diabetes, the 75-g, 2 h oral glucose tolerance test (OGTT) during the first pregnancy visit was given and for those with negative result, test was repeated in 24–28th weeks of gestation. At the time of data collection, women were asked about their history of GDM based on a self-reporting questionnaire.

The American Diabetes Association criteria for T2DM, IGT and IFG definitions were utilized [16]; T2DM: using anti-diabetic drugs or FBS ≥ 7 mmol/l (measured twice) or 2 h plasma glucose (OGTT)) ≥ 11.1 mmol/l.