Original Article

Incidence of Prediabetes/Diabetes among Women with Prior Gestational Diabetes and Non-Alcoholic Fatty Liver Disease: A Prospective Observational Study

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Abstract

Background and Objectives: This prospective longitudinal study aims to evaluate and compare the incidence of prediabetes/diabetes among women stratified at the baseline postpartum visit according to the prior GDM and NAFLD status. **Methods:** Of the 309 women with baseline postpartum assessment at a median of 16 months following the index delivery, 200 (64.7%) [GDM: 137 (68.5%), normoglycaemia: 63 (31.5%)] were available for the follow-up analysis (performed at median of 54 months following the index delivery) and were participants for this study. We obtained relevant demographic, medical and obstetric details and performed a 75 g OGTT with glucose estimation at 0 and 120 min. NAFLD status was defined by ultrasonography at the baseline visit. Participants were divided into four groups: no NAFLD and no prior GDM (group 1), NAFLD but no prior GDM (group 2), prior GDM but no NAFLD (group 3), and NAFLD and prior GDM (group 4). **Results:** The mean age of study participants (n = 200) was 32.2 ± 5.1 years, and the mean interval between the two visits was 34.8 ± 5.5 months. A total of 74 (37%) women had progression to prediabetes/diabetes [incidence rate of 12.8/100 woman-years]. The incidence rates (per 100 woman-years) were 8.6, 8.9, 13.4 and 15.3 in groups 1, 2, 3 and 4, respectively. The adjusted hazard ratio for incident (new-onset) prediabetes/diabetes in group 4 (reference: group 1) was 1.99 (95% CI 0.80, 4.96, $P = 0.140$). Among women with baseline NAFLD (irrespective of GDM status), the risk of incident prediabetes/diabetes increased with an increase in the duration of follow-up (3.03-fold higher per year of follow-up, $P = 0.029$) and was significantly higher in women who were not employed (6.43, 95% CI 1.74, 23.7, $P = 0.005$) and in women with GDM requiring insulin/metformin during pregnancy (4.46, 95% CI 1.27, 15.64, $P = 0.019$). **Conclusion:** NAFLD and GDM increased the risk for glycaemic deterioration in young Indian women. Future studies should focus on evaluating the effectiveness of lifestyle and behavioural interventions in such high-risk women.

Keywords: Diabetes, GDM, incidence, NAFLD, South Asian, women

Introduction

Non-alcoholic fatty liver disease (NAFLD) is considered as the hepatic component of metabolic syndrome and has emerged as one of the most common causes of chronic liver disease worldwide.[1] This condition has a high global prevalence, affecting nearly one in every four individuals.[2] A recent meta-analysis from India suggests NAFLD to be present in one in every three Indians.[3] The prevalence is even higher (nearly one in every two adults) in high-risk groups such as type 2 diabetes and women with previous gestational diabetes (GDM).[3-5] Apart from cirrhosis, NAFLD is associated with increased risk of cardiovascular diseases, certain cancers, obstructive sleep apnoea and various endocrinopathies, including diabetes.[1] A meta-analysis of 33 observational studies found a hazard ratio of 2.2 [95% CI 1.9-2.5] for incident diabetes in individuals with NAFLD compared to those without it.[6] Furthermore, NAFLD is independently is associated with increased risk for both macrovascular

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Submitted: 12-Feb-2023 **Revised:** 12-Mar-2023
Accepted: 21-Mar-2023 **Published:** 28-Aug-2023

How to cite this article: Gupta Y, Kubihal S, Shalimar, Kandasamy D, Goyal A, Goyal A, *et al*. Incidence of prediabetes/diabetes among women with prior gestational diabetes and non-alcoholic fatty liver disease: A prospective observational study. Indian J Endocr Metab 2023;27:319-24.

Supplementary material available online

Access this article online

Quick Response Code:

Website: https://journals.lww.com/indjem/

DOI: 10.4103/ijem.ijem_60_23

and microvascular complications of diabetes (especially nephropathy and neuropathy).[7]

The high burden of NAFLD and its striking association with incident diabetes and diabetes-related vascular complications highlight the need to screen this disease in high-risk individuals. Women with GDM constitute one such high-risk group, where the risk for diabetes is nearly 10-fold higher compared to women with normoglycaemia in pregnancy.[8] Previously, we reported a high prevalence of dysglycaemia (57.7%: 10.5% diabetes and 47.2% prediabetes) among women with prior GDM.[9] In another study, we found that the prevalence of NAFLD was strikingly elevated at 62.7% in women with prior GDM.[5] Although there are data on adverse pregnancy outcomes among women with GDM and NAFLD,[10,11] to the best of our literature review, there are no data on incident diabetes among such women. Therefore, the current study was performed to address this literature gap. We aimed to study the incidence of prediabetes/diabetes (i.e., change in glycaemic category from normoglycaemia to prediabetes/diabetes, or from prediabetes to diabetes) among women with NAFLD and prior GDM.

Methods

Settings and study design

The data collection for this prospective observational longitudinal study was carried out from May 2018 to April 2022 (May 2018 to November 2019 for the baseline postpartum visit; December 2019 to April 2022 for the follow-up visit) after obtaining approval from the ethics committee of the institution, and written informed consent from the participating women.

Objectives

This study aims to report the incidence of prediabetes/diabetes and changes in other cardiometabolic risk factors (blood pressure, lipid and weight-related parameters) in the women stratified at baseline postpartum visit according to the prior GDM status and the presence of NAFLD. Our primary objective was to compare the new-onset diabetes/prediabetes in these four groups: no NAFLD and no prior GDM (group 1 or reference group, n = 33), NAFLD but no prior GDM (group 2, n = 30), prior GDM but no NAFLD (group 3, n = 48), and NAFLD and prior GDM (group 4, n = 89). The secondary objectives were as follows: (i) to evaluate and compare the changes in other cardiometabolic risk factors in these four groups and ii) to evaluate factors associated with glycaemic category progression in women with NAFLD.

Inclusion and exclusion criteria

All women (n = 309) evaluated at the baseline postpartum visit (at a median of 16 months following the index delivery) for NAFLD status were eligible for this study.[5] This included 201 (65%) women with GDM and 108 (35%) women with normoglycaemia per the IADPSG criteria in their index pregnancy between 2012 and 2019 and who were at least 6 months postpartum at the baseline evaluation. Of these 309 women, 200 (64.7%) [GDM: 137 (68.5%), normoglycaemia in pregnancy: 63 (31.5%)] were available for the follow-up analysis (performed at median of 54 months following the index delivery) and were participants for this study. The diagnosis of GDM or normoglycaemia was ascertained through hospital records and was not based on recall. In the baseline assessment, we excluded women with hyperglycaemia other than GDM in their index pregnancy, such as overt diabetes in pregnancy or pre-existing diabetes mellitus, and those who had diabetes or were pregnant at the time of study evaluation. We also excluded women with hepatitis B or hepatitis C infection, a history of significant alcohol intake (>14 drinks/week; each drink: 10 g of alcohol) and a history of steroid intake in the past year (except for the indication of foetal lung maturation during the antenatal period). Other exclusion criteria included a history of significant organ impairment, chronic infections, connective tissue disorders, chronic inflammatory conditions and intake of other drugs known to cause hepatic steatosis.

Participant recruitment and procedure on the day of testing

We invited participants to attend the centre in a fasting state (minimum fast of 10 h). A relevant medical history, along with an assessment of anthropometric and biochemical parameters, was performed. The detailed methodology on oral glucose tolerance test (OGTT), collection, transportation and analysis of samples, along with details on anthropometric methods, is available in our previous publications.[5,12]

Definitions

We defined prediabetes and diabetes per the American Diabetes Association criteria and overweight and obesity per the World Health Organization criteria.[13,14] Glycaemic progression was defined as a change in category from a) normoglycaemia to prediabetes, b) normoglycaemia to diabetes and c) prediabetes to diabetes. Diabetes was defined if any of the three parameters crossed the diagnostic threshold (i.e., fasting plasma glucose ≥7 mmol/L or 126 mg/dl or 2-h plasma glucose ≥11.1 mmol/L or 200 mg/dl or HbA1c ≥6.5%). For research purposes, the diagnosis of diabetes was made even if one value was abnormal.

Algorithm for the diagnosis of NAFLD

All study participants (cases and controls) underwent abdominal ultrasonography (USG). Abdominal USG was performed after a 10-h fast using the Supersonic Aixplorer Imagine (Supersonic, Aix-en-Provence, France) USG machine with a curvilinear probe (2–5 MHz). One of the two consultant radiologists (DK and AnG) carried out the scan and were blinded to the clinical data of the study participants. NAFLD was defined using a standard method at the baseline postpartum visit.[15] Normal liver parenchyma has a homogeneous echotexture with echogenicity equal to or slightly higher than that of the renal cortex and spleen. Hepatic steatosis severity was graded as: grade 0, normal echogenicity; grade 1, diffusely increased hepatic echogenicity, but appreciable periportal and diaphragmatic echogenicity; grade 2, diffusely increased hepatic echogenicity obscuring periportal echogenicity, but

appreciable diaphragmatic echogenicity; and grade 3, diffusely increased hepatic echogenicity obscuring periportal and diaphragmatic echogenicity.[5,15]

Sample size calculation

This study intended to include all participants from the baseline evaluation.[5] Therefore, we did not calculate the sample size *apriori*. The enrolled participants and observed event rates provided post hoc power of 92.9% (with an alpha error of 0.05) for the differences in the progression of glycaemia between the following two extreme groups: a) women with normoglycaemia in pregnancy and no NAFLD (group 1), and b) women with prior GDM and NAFLD (group 4).

Statistical analysis

We carried out statistical analysis using Stata 15.0 (StataCorp, College Station, TX, USA). Data are presented as the number (%), mean ± standard deviation or median (interquartile range [IQR]), as appropriate. We calculated crude and adjusted hazard ratio (HR) for incident prediabetes/diabetes using Cox proportional hazards model. Factors having a strong bearing on the outcome (progression of glycaemic category) such as age, postpartum body mass index (overweight/obesity: yes/no) and family history of diabetes were taken as covariates in the adjusted model. We calculated the incidence rates for prediabetes/diabetes per 100 woman-years for different groups. We used multivariate logistic regression analysis to evaluate factors associated with worsening of glycaemic category in women with NAFLD (including both women with and without GDM) and expressed results as odds ratio (95% confidence interval [CI]). Since age >35 years is a risk factor for incident diabetes, and weight gain of >5% is traditionally considered as significant, we used these as dichotomous variables in the logistic regression analysis. We calculated the change in cardiometabolic risk factors between the two visits and compared the differences among different categories. The women with normoglycaemia during pregnancy and who had no NAFLD (group 1) were used as the reference category for the analysis. The significance level was set at $P < 0.05$.

Ethical Clearance Statement

The ethics committee of the institution (All India Institute of Medical Sciences, New Delhi) approved the protocol (Ref. No. IECPG-166/19.04.2018, dated 23 April 2018). The work started after the ethics approval, and it conforms to the provisions of the Declaration of Helsinki (as revised in Fortaleza, Brazil, October 2013).

Results

Baseline characteristics

A total of 200 participants who were enrolled in the cohort at a median (IQR) postpartum interval of 17 (8-39) months were available for this longitudinal study. The baseline characteristics of study participants are presented in Table 1. In a sensitivity analysis comparing baseline visit characteristics of participants who were available (n = 200) and not available for the follow-up (n = 109) evaluation, the participants with follow-up assessment had significantly higher plasma glucose levels (120 min post-load), glycated haemoglobin, BMI and prevalence of prediabetes [Supplementary Table 1].

Table 1: Baseline characteristics of study participants

Variable	Total (*n*=200)
Age at current testing (years)	32.2±5.1
Working status, employed	36 (18%)
Education, graduate or above	133 (66.5%)
Family history of diabetes	77 (38.5%)
Number of live births ≥2	97 (48.5%)
Diagnosis of GDM	
First trimester	27 (13.7%)
Second trimester	141 (71.6%)
Third trimester	29 (14.7%)
Insulin or metformin use during pregnancy[a]	29 (21.2%)
Time since last delivery (months)	17 (8-39)
Time interval between two visits (months)	34.8±5.5

Data are presented as mean±SD, median (IQR) or *n* (%), [a]n=137.
GDM: Gestational diabetes mellitus

The mean (±SD) age of study participants at the current evaluation was 32.2 ± 5.1 years, and the mean interval between the two visits was 34.8 ± 5.5 months. A total of 36 (18%) women were employed, and 133 (66.5%) had education until graduation or above. Of the 137 women with prior GDM, 89 (65%) had NAFLD; on the other hand, of the remaining 63 with normoglycaemia in pregnancy, 30 (47.6%) had NAFLD. A history of insulin/metformin use was present in 29 (21.2%) women with GDM [Table 1].

Incidence of prediabetes/diabetes in study participants

Seventy-four (37%) women progressed: normoglycaemia to prediabetes in 56 (28%) women, normoglycaemia to diabetes in three (1.5%) women and prediabetes to diabetes in 15 (7.5%) women [Table 2]. The overall incidence of prediabetes/diabetes was 12.8 per 100 woman-years. The proportion who had glycaemic category progression was significantly higher in women with prior GDM and NAFLD (39/89: 43.8% in group 4) compared to those with no prior GDM and no NAFLD (8/33: 24.2% in group 1) (P = 0.048). The proportion who had glycaemic category progression in groups 2 and 3 were 26.7% (8/30) and 39.6% (19/48), respectively. The incidence of prediabetes/diabetes was also higher in group 4 (15.3 per 100 woman-years) compared to group 1 (8.6 per 100 woman-years). The unadjusted HR and adjusted HR for incident prediabetes/diabetes in group 4 were 2.01 (95% CI 0.85, 4.76, P = 0.112) and 1.99 (95% CI 0.80, 4.96, P = 0.140), respectively (reference category: group 1) [Table 3].

A total of 18 (9%) women progressed to diabetes (normoglycaemia to diabetes: n = 3 and prediabetes to diabetes, n = 15). Notably, all of these women belonged to groups 3 and 4, i.e., had a history of prior GDM with or

Table 2: Glycaemic category progression and incidence of prediabetes/diabetes in different study groups stratified according to prior GDM and NAFLD status at the baseline postpartum visit

Variable	Total (*n*=200)	Group 1 (*n*=33)	Group 2 (*n*=30)	Group 3 (*n*=48)	Group 4 (*n*=89)
NG to PD	56 (28%)	8 (24.2%)	8 (26.7%)	13 (27.1%)	27 (30.3%)
NG to T2D	3 (1.5%)	0	0	1 (2.1%)	2 (2.2%)
PD to T2D	15 (7.5%)	0	0	5 (10.4%)	10 (11.2%)
Overall progression	74 (37%)	8 (24.2%)	8 (26.7%)	19 (39.6%)	39 (43.8%)
Incidence rate/100 woman-years	12.8	8.6	8.9	13.4	15.3

Group 1: No NAFLD and no prior GDM, Group 2: NAFLD but no prior GDM, Group 3: Prior GDM but no NAFLD, Group 4: NAFLD and prior GDM. GDM: Gestational diabetes mellitus, NAFLD: Non-alcoholic fatty liver disease, NG: Normoglycaemia, PD: Prediabetes, T2D: Type 2 diabetes mellitus

Table 3: Unadjusted and adjusted hazard ratio (95% CI) for incident prediabetes/diabetes in different study groups

Variable	Unadjusted	Adjusted*
Group 1	1.0 (Ref.)	1.0 (Ref.)
Group 2	0.95 (0.33, 2.75) *P*=0.923	0.94 (0.32, 2.76) *P*=0.911
Group 3	1.64 (0.66, 4.12) *P*=0.289	1.61 (0.63, 4.12) *P*=0.319
Group 4	2.01 (0.85, 4.76) *P*=0.112	1.99 (0.80, 4.96) *P*=0.140

Group 1: No NAFLD and No prior GDM, Group 2: NAFLD but no prior GDM, Group 3: Prior GDM but no NAFLD, Group 4: NAFLD and prior GDM. *Covariates adjusted: age, postpartum body mass index (overweight/obesity: yes/no) and family history of diabetes

without NAFLD. The incidence rate for diabetes was higher in women with prediabetes (7.34 per 100 woman-years) compared to normoglycaemia (0.80 per 100 woman-years) at the baseline visit.

Factors associated with incident prediabetes/diabetes in women with NAFLD at baseline

In the multivariate logistic regression model (analysis restricted only to women with NAFLD on USG), we found that the risk of incident prediabetes/diabetes significantly increased with an increase in the duration of follow-up (3.03-fold higher per year of follow-up, $P = 0.029$). The risk was also higher in women who were not employed (or homemakers) compared to those who were employed (6.43, 95% CI 1.74, 23.7, $P = 0.005$) and in women with GDM who required insulin/metformin during pregnancy (4.46, 95% CI, 1.27, 15.64, $P = 0.019$). The risk was also higher by more than twofold in women with age >35 years, and those with weight gain of >5% between the two visits; however, this did not reach statistical significance [Table 4].

Changes in other cardiometabolic parameters between two visits among study participants

The delta changes in other cardiometabolic parameters such as weight, body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides were not significantly different between groups 2-4 and group 1 (reference group) [Supplementary Table 2].

Table 4: Factors associated with incident prediabetes/diabetes among women with baseline NAFLD on logistic regression analysis (adjusted for GDM status)

Variable	Bivariate OR (95% CI)	*P*
Age >35 years	2.54 (0.95-6.84)	0.065
Occupation (Not Employed)	6.43 (1.74-23.7)	0.005
Education (Less than graduate)	1.66 (0.60-4.59)	0.331
Family history of diabetes present	1.81 (0.71-4.62)	0.212
Use of insulin/metformin during pregnancy	4.46 (1.27-15.64)	0.019
BMI ≥25 kg/m^2	1.70 (0.63-4.57)	0.296
Live births >1	1.43 (0.57-3.62)	0.449
Weight gain of >5%	2.03 (0.75-5.52)	0.165
Duration of follow up (per 1 year increase)	3.03 (1.12-8.23)	0.029

BMI: Body mass index

Discussion

In this longitudinal study, we evaluated and compared the incidence of prediabetes/diabetes among women stratified at the baseline postpartum visit according to the prior GDM and NAFLD status. We found that at a mean follow-up interval of 35 months, a significantly higher proportion of women with prior GDM and NAFLD (group 4) progressed to prediabetes/diabetes compared to those without prior GDM and no NAFLD (group 1) at baseline. A total of 18 (9%) women had incident diabetes, and all these events occurred in women with prior GDM (groups 3 and 4). In the multivariate logistic regression model involving women with NAFLD at baseline (groups 2 and 4), the risk for glycaemic progression was significantly higher in homemakers, those who required insulin/metformin therapy during the index pregnancy and the risk further increased with each 1-year increase in the interval between the two study visits. On the other hand, we did not find any significant difference in the delta changes in blood pressure and lipid parameters between any of the study groups and the reference group or group 1.

We found the highest risk [adjusted HR 1.99; 95% CI 0.80, 4.96, $P = 0.140$)] for incident prediabetes/diabetes in women with NAFLD and prior GDM (reference: women with no NAFLD and no prior GDM). A recent and updated meta-analysis of 33 studies including 501022 participants (30.8% with NAFLD) reported a 2.2-fold increased risk of incident diabetes in

individuals with NAFLD over a median follow-up of 5 years.[6] The risk was higher in individuals with more severe forms of NAFLD (HR 2.7) and in studies with follow-up duration of >5 years, compared to <5 years (HR 2.37 vs. 1.96). Our study had a mean follow-up duration of approximately 3 years, and the risk may further increase on a longer follow-up, as suggested by the results of this meta-analysis.

We found a strong association between employment and the risk of incident diabetes in women with NAFLD at baseline, as homemakers were at high risk for worsening glycaemic status. Ogungbe *et al*.[16] reported similar findings. Job contributes to the social security of the family from a financial perspective. Most of the women in our study come from economically weaker strata, which may be one reason for the positive impact of employment. However, this observation needs further validation in larger cohorts involving young women with a history of recent childbirth. We also found a higher risk for incident glycaemic progression in women who needed insulin/metformin in their index pregnancy. The need for pharmacotherapy indicates a more severe form of GDM and is known to be associated with a higher postpartum diabetes risk.[9] The interval between the two study visits was another significant predictor for worsening glycaemia in line with the findings from the meta-analysis discussed previously.[6]

The presence of NAFLD is associated with an increased risk of incident hypertension. A recent meta-analysis of 11 cohort studies with 390 348 participants found that NAFLD is associated with a 1.6-fold increased risk of incident hypertension.[17] The risk decreased to HR of 1.36 (95% confidence interval (CI), 1.20-1.54) when adjusted for adiposity. Overall, the risk was lower in studies reporting NAFLD using imaging methods compared to blood biomarkers, those with follow-up duration of <6 years compared to >6 years, and those performed in Asia compared to Europe/USA. We did not report incident hypertension separately due to a small number of events. In our analysis, the difference in delta changes in systolic and diastolic blood pressure between the two study visits among the various groups was not different. As suggested by one of the meta-analyses, NAFLD has a high prevalence of dyslipidaemia.[18] NAFLD is characterised by atherogenic dyslipidaemia, comprising of high triglyceride, low high-density lipoprotein cholesterol (HDL-C) and increased small dense low-density lipoprotein (LDL) particles.[19] Dyslipidaemia is an essential mediator between NAFLD and cardiovascular disease.[20] Similar to blood pressure parameters, the delta changes in the lipid parameters between the study visits among different arms were not different. This lack of meaningful difference in blood pressure and lipid parameters could be ascribed to the young age of our study cohort and a relatively short follow-up period of 3 years. The duration and severity of NAFLD may also be comparatively lesser at this stage.

The strengths of our study are its longitudinal design, the inclusion of a young South Asian population and comprehensive evaluation of cardiometabolic risk profile with a standard methodology at both the study visits. Most published data for incident diabetes among individuals with NAFLD have come from relatively older individuals, and studies performed in East Asia and other developed countries.[6] To the best of our literature review, ours is the first study to report the incidence of diabetes/prediabetes in South Asian women with prior GDM and NAFLD, two high-risk conditions portraying an increased risk of future diabetes. We acknowledge some limitations. The sample size was small. The follow-up duration was around 3 years, which informed significant differences in the progression of glycaemic categories. Still, it may have been insufficient to capture meaningful changes in other cardiometabolic parameters such as blood pressure and lipid profile. The sensitivity analysis suggested that women with worse cardiometabolic profile were more likely to return for follow-up, and thus, the overall incidence may have been an overestimate. Study participants were recruited from a tertiary care centre, so the results may not be generalisable to the community at large, and a large population-based study with extended follow-up will be needed in this regard.

To conclude, we report a higher incidence of glycaemic progression at a mean follow-up of 35 months among women with NAFLD and GDM, compared to their counterparts with no NAFLD and normoglycaemia in pregnancy. There was no meaningful clinical progression in blood pressure or lipid parameters in our cohort. Thus, NAFLD and prior GDM increased the risk for glycaemic deterioration in young Indian women, and we propose that future studies should focus on evaluating the effectiveness of lifestyle and behavioural interventions in these high-risk women.

Ethics statement

The data collection for this prospective observational longitudinal study was carried out from May 2018 to April 2022 at All India Institute of Medical Sciences, New Delhi, India (a public tertiary care hospital catering predominantly to a low- and middle-income population), after obtaining approval from the ethics committee of the institution, and written informed consent from the participating women.

Acknowledgements

The authors thank study participants for generously donating their time and information.

Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Informed Consent

All women gave written informed consent for participation and use of the patient data for research and educational purposes.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Supplementary Material

Supplementary Table 1: Sensitivity analysis comparing baseline characteristics of women who were available and not available for the follow-up assessment

Variable	Not available (n=109)	Available (n=200)	p value
Age (years)	31.4±4.8	32.2±5.1	0.170
Postpartum interval (months)	14 (9-31)	17 (8-39)	0.395
Occupation (Employed)	24 (22.0)	36 (18.0)	0.394
Graduate and above	74 (67.9)	133 (66.5)	0.804
Family history of diabetes	39 (35.8)	77 (38.5)	0.637
Use of insulin/metformin in pregnancy	14 (12.8)	30 (15.1)	0.593
BMI (kg/m^2)	25.5±4.8	26.7±4.5	**0.042**
Prediabetes	44 (40.4)	106 (53.0)	**0.034**
Plasma glucose (0 min) (mmol/L)	5.0±0.5	5.1 ±0.6	0.134
Plasma glucose (120 min) (mmol/L)	6.0±1.4	6.5±1.6	**0.006**
HbA1c (%)	5.4±0.4	5.5±0.4	**0.041**
SBP (mm Hg)	107.2±11.3	106.1±10.8	0.406
DBP (mm Hg)	72.0±8.7	71.8±9.2	0.817
TC(mmol/L)	4.4±1.0	4.4±0.8	0.882
LDL-C(mmol/L)	2.6±0.9	2.6±0.7	0.761
HDL-C(mmol/L)	1.3±0.3	1.3±0.3	0.544
TG(mmol/L)	1.2±0.5	-1.2±0.5	0.154

SBP: Systolic blood pressure, DBP: Dystolic blood pressure, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, TC: Total Cholesterol, TG: Triglycerides, BMI: Body mass index; HbA1c: Hemoglobin A1c

Supplementary Table 2: Differences in cardiometabolic risk factors between two visits among women in different study groups stratified according to prior GDM and NAFLD status at the baseline postpartum visit

Variable	Group 1 (n=33)	Group 2 (n=30)	Group 3 (n=48)	Group 4 (n=89)
Plasma glucose (0 min) (mmol/L)				
Baseline	4.8±0.4	4.9±0.5	5.1±0.6	5.3±0.6
Follow-up	5.1±0.4	5.2±0.5	5.8±1.0	5.8±0.9
Delta (Pre-Post)	0.37±0.10	0.31±0.08	0.72±0.86	0.57±0.72
P value	Reference	0.638	0.046	0.163
Plasma glucose (120 min) (mmol/L)				
Baseline	5.6±1.5	6.0±1.1	6.2±1.5	7.1±1.6
Follow-up	5.9±1.2	6.3±1.3	6.9±2.1	7.9±2.4
Delta (Pre-Post)	0.33±1.49	0.35±1.25	0.78±1.83	0.69±2.24
P value	Reference	0.950	0.268	0.415
HbA1c (%)				
Baseline	5.3±0.3	5.3±0.4	5.5±0.4	5.6±0.4
Follow-up	5.2±0.3	5.3±0.4	5.6±0.7	5.7±0.6
Delta (Pre-Post)	-0.10±0.26	-0.02±0.28	0.09±0.49	0.06±0.53
P value	Reference	0.252	0.046	0.089
SBP (mm Hg)				
Baseline	103.5±8.4	106.2±12.6	105.3±9.4	107.6±11.4
Follow-up	107.9±10.2	107.6±10.7	110.2±9.7	112.6±11.5
Delta (Pre-Post)	4.36±8.60	1.40±9.72	4.86±9.49	4.77±9.26
P value	Reference	0.204	0.810	0.587
DBP (mm Hg)				
Baseline	69.7±7.3	73.1±9.9	70.6±8.7	73.1±9.7
Follow-up	73.4±7.8	71.6±9.1	73.3±7.5	74.9±9.2
Delta (Pre-Post)	3.73±8.73	-1.10±10.45	2.55±9.35	1.91±8.04

Contd...

Supplementary Table 2: Contd...

Variable	Group 1 (n=33)	Group 2 (n=30)	Group 3 (n=48)	Group 4 (n=89)
P value	Reference	0.052	0.572	0.141
TC (mmol/L)				
Baseline	4.3±1.1	4.4±0.7	4.4±0.7	4.5±0.8
Follow-up	4.3±1.1	4.3±0.7	4.5±0.9	4.4±0.8
Delta (Pre-Post)	-0.06±9.11	-0.14±0.56	0.11±0.63	-0.06±0.68
P value	Reference	0.678	0.309	0.506
LDL-C (mmol/L)				
Baseline	2.5±0.9	2.5±0.6	2.6±0.6	2.7±0.6
Follow-up	2.3±0.8	2.4±0.6	2.7±0.8	2.6±0.7
Delta (Pre-Post)	-0.15±0.70	-0.11±0.47	0.07±0.56	-0.11±0.58
P value	Reference	0.771	0.118	0.644
HDL-C (mmol/L)				
Baseline	1.4±0.4	1.3±0.3	1.2±0.2	1.2±0.3
Follow-up	1.5±0.4	1.3±0.3	1.2±0.2	1.2±0.3
Delta (Pre-Post)	0.04±0.30	-0.05±0.24	0.03±0.23	0.04±0.23
P value	Reference	0.225	0.875	0.542
TG (mmol/L)				
Baseline	1.0±0.3	1.2±0.5	1.2±0.5	1.4±0.6
Follow-up	1.1±0.5	1.3±0.5	1.3±0.4	1.4±0.6
Delta (Pre-Post)	0.13±0.48	0.06±0.52	0.05±0.35	0.03±0.48
P value	Reference	0.556	0.361	0.141
Waist circumference (cm)				
Baseline	85.1±7.4	94.3±11.4	88.6±11.2	95.0±10.6
Follow-up	87.0±8.6	93.2±11.9	90.9±11.0	94.9±10.4
Delta (Pre-Post)	1.44±7.87	-1.08±6.65	2.27±6.83	-0.25±7.35
P value	Reference	0.180	0.616	0.278
BMI (kg/m^2)				
Baseline	23.8±3.0	26.7±4.5	25.6±4.4	28.2±4.6
Follow-up	24.7±3.5	27.4±4.3	26.4±4.3	28.1±5.3
Delta (Pre-Post)	0.85±2.02	0.70±2.15	0.84±1.59	-0.08±3.48
P value	Reference	0.776	0.977	0.153
Weight (kg)				
Baseline	58.3±8.1	62.3±11.3	63.1±12.5	67.1±11.9
Follow-up	60.5±9.4	64.1±11.7	65.0±11.7	67.0±13.5
Delta (Pre-Post)	2.11±5.08	1.74±5.11	1.98±3.89	-0.21±8.53
P value	Reference	0.771	0.898	0.144

Group 1: no NAFLD and no prior GDM; Group 2: NAFLD but no prior GDM; Group 3: prior GDM but no NAFLD; Group 4: NAFLD and prior GDM. SBP: Systolic blood pressure, DBP: Dystolic blood pressure, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, TC: Total Cholesterol; TG: Triglycerides; BMI: Body mass index