

From Gestational Diabetes to Fatty Liver: Tracking the Journey to Prediabetes and Diabetes in Women – A Prospective Observational Study

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Abstract:

Background: Gestational diabetes mellitus (GDM) and non-alcoholic fatty liver disease (NAFLD) are recognized risk variables for the development of prediabetes and diabetes. Understanding the combined effect of these conditions on the progression to glucose intolerance is crucial for developing effective prevention strategies. The study aimed to examine the incidence of prediabetes and diabetes in females with a history of GDM and NAFLD, in contrast to those with only one or neither condition, and to identify key risk factors related with these outcomes.

Methods: 200 women were enrolled in a prospective observational study and allocated into four groups: Group A (GDM only), Group B (NAFLD only), Group C (both GDM and NAFLD), and Group D (control group with neither condition). Participants were followed for two years, with incidence rates of prediabetes and diabetes recorded. Baseline characteristics were assessed, and Cox proportional hazards models were used to identify significant risk factors.

Results: The highest incidence of prediabetes and diabetes was observed in Group C, with 60% developing prediabetes and 50% developing diabetes. Group A had 40% prediabetes and 20% diabetes incidence, Group B had 36% and 24%, respectively, and Group D had 20% and 10%. Higher BMI, family history of diabetes, history of GDM, and presence of NAFLD were significant risk factors, while healthy dietary habits were protective.

Conclusion: Females with a history of both GDM and NAFLD are at a considerably higher risk of developing prediabetes and diabetes. These findings underline the importance of targeted prevention and early intervention strategies in this high-risk population.

Recommendations: Healthcare providers should prioritize monitoring and managing women with both GDM and NAFLD to prevent the onset of prediabetes and diabetes. Regular screening and promoting healthy lifestyle modifications are essential to mitigate these risks.

Keywords: Gestational Diabetes Mellitus, Non-Alcoholic Fatty Liver Disease, Prediabetes, Diabetes, Risk Factors, Preventive Strategies

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Introduction

Type 2 diabetes mellitus (T2DM) and other metabolic disorders are greatly increased by two common conditions: non-alcoholic fatty liver disease (NAFLD) and gestational diabetes mellitus (GDM). Glucose intolerance initially detected during pregnancy is the hallmark of GDM, which affects about 7% of pregnancies globally [1]. Conversely, NAFLD is the most prevalent chronic liver disease worldwide, impacting almost one-third of the population and linked to obesity, insulin resistance, and metabolic syndrome [2].

Women who have experienced GDM are at a heightened risk of developing T2DM in the years following pregnancy, with studies indicating that nearly 50% of females with GDM will develop T2DM within ten years [3]. Similarly, NAFLD is a significant predictor of T2DM due to its close association with insulin resistance and chronic inflammation. The coexistence of GDM and NAFLD in women may have a synergistic effect, substantially increasing the risk of progressing to prediabetes and T2DM. However, there is limited research exploring the combined impact of these conditions on metabolic outcomes.

Recent studies have underscored the importance of early identification and management of these high-risk individuals to prevent the onset of T2DM and its complications [4]. Interventions such as lifestyle modifications, including diet and physical activity, have been shown to significantly lower the risk of development to T2DM in females with a history of GDM [5]. Despite this, the role of NAFLD in this high-risk group remains underexplored, necessitating further investigation into effective prevention and management strategies.

Understanding the combined impact of GDM and NAFLD is essential for healthcare providers to implement effective screening, prevention, and management strategies. As the incidence of both

conditions continues to rise globally, this research becomes increasingly relevant for addressing the burgeoning epidemic of T2DM and metabolic disorders in women.

The current study aimed at investigating the incidence of prediabetes and diabetes in women with a history of gestational diabetes mellitus and non-alcoholic fatty liver disease.

Methodology:

Study Design

A prospective observational study.

Study Setting

The study was conducted at the tertiary care hospital. The study spanned a period of six months.

Participants

A total of 200 women were enrolled in the study. Participants were allocated into four groups based on specific criteria:

1. Group A: Women with a history of GDM only (n=50)
2. Group B: Women with a history of NAFLD only (n=50)
3. Group C: Women with both GDM and NAFLD (n=50)
4. Group D: Control group - Women with neither GDM nor NAFLD but with similar demographic characteristics (n=50)

Inclusion Criteria:

- Women aged 20-50 years.
- History of gestational diabetes mellitus.
- -Diagnosis of NAFLD confirmed by ultrasonography or liver biopsy for Groups B and C.
- No history of GDM or NAFLD for Group D.
- -Willingness to participate and provide informed consent.

Exclusion Criteria:

- Pre-existing diabetes before pregnancy.
- Chronic liver diseases other than NAFLD.

- Use of drugs that may have an impact on glucose metabolism.
- Pregnant or planning pregnancy during the study period.

Ethical considerations:

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Sample size:

To calculate the sample size for this study, the following formula was used for estimating a proportion in a population:

$$n = \frac{Z^2 \times p \times (1-p)}{E^2}$$

Where:

- n = sample size
- Z = Z-score corresponding to the desired level of confidence
- p = estimated proportion in the population
- E = margin of error

Bias

To minimize selection bias, participants were randomly selected from the eligible population visiting the clinics. Information bias was reduced by using standardized data collection procedures.

Variables

Variables included history of GDM, presence of NAFLD, age, BMI, family history of diabetes, physical activity levels, dietary habits, incidence of prediabetes, incidence of diabetes.

Data Collection:

Data were collected through a combination of medical record reviews, patient interviews, and physical examinations. Baseline data included demographic information, medical history, and lifestyle factors.

Procedure:

1. Eligible participants were identified and contacted during their routine clinic visits. Informed consent was obtained.
2. Initial assessments included detailed medical record, physical examination, and laboratory tests (e.g., fasting blood glucose, HbA1c, liver function tests).
3. Participants were followed up every six months. At each visit, fasting blood glucose and HbA1c levels were evaluated. Additional tests, such as oral glucose tolerance tests (OGTT), were performed as needed to diagnose prediabetes and diabetes.
4. All data were recorded in a secure, electronic database with restricted access to ensure confidentiality.

Statistical Analysis:

Version 20.0 of the SPSS software was used to analyse the data. The relationship between baseline characteristics and the onset of prediabetes or diabetes was evaluated using Cox proportional hazards models. Statistical significance was attained when the p-value was less than 0.05.

Ethical considerations:

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Result:

Table 1 provides a summary of the 200 participants' baseline characteristics. The participants' average age was 35 years (\pm 5.6 years), and there was no substantial variation among the four groups. The BMI, physical activity levels, food preferences, and family history of diabetes were also similar amongst the groups, guaranteeing an even distribution of important lifestyle and demographic variables.

Table 1: Baseline Characteristics of Participants

Characteristic	Group A	Group B	Group C	Group D	p-value
Age (years)	34.8 ± 5.4	35.2 ± 5.9	34.7 ± 5.3	35.1 ± 5.8	0.89
BMI (kg/m ²)	27.6 ± 3.2	28.1 ± 3.4	28.3 ± 3.6	27.8 ± 3.1	0.78
Family History of DM (%)	30	28	32	27	0.67
Physical Activity (%)	60	55	58	62	0.80
Dietary Habits (Healthy)	70	68	65	72	0.82

Over the follow-up period of two years, the incidence of prediabetes and diabetes was recorded. The highest incidence was observed in Group C (GDM + NAFLD), with 60% developing prediabetes and 50% developing diabetes. Group A (GDM Only) had a prediabetes incidence of 40% and a diabetes incidence of 20%. Group B (NAFLD Only) showed a prediabetes

incidence of 36% and a diabetes incidence of 24%. The control group (Group D) had the lowest incidence, with 20% developing prediabetes and 10% developing diabetes. These differences were statistically substantial ($p < 0.01$), implying a strong relationship between the combined history of GDM and NAFLD and the development of prediabetes and diabetes

Table 2: Incidence of Prediabetes and Diabetes

Characteristic	Group A	Group B	Group C	Group D	p-value
Prediabetes (%)	20 (40%)	18 (36%)	30 (60%)	10 (20%)	<0.01
Diabetes (%)	10 (20%)	12 (24%)	25 (50%)	5 (10%)	<0.01

Cox proportional hazards models were used to assess the risk factors related with the development of prediabetes and diabetes. Significant risk factors included higher BMI (HR = 1.15, $p < 0.01$), family history of diabetes (HR = 1.40, $p < 0.01$), history of GDM (HR = 1.50, $p < 0.01$), and presence

of NAFLD (HR = 1.65, $p < 0.01$). Healthy dietary habits had a protective effect (HR = 0.78, $p = 0.01$). Physical activity showed a trend towards a protective effect but was not statistically significant (HR = 0.85, $p = 0.07$

Table 3: Risk Factors for Prediabetes and Diabetes (Cox Proportional Hazards Model)

Variable	Hazard Ratio (HR)	95% Confidence Interval	p-value
Age	1.02	0.98-1.06	0.28
BMI	1.15	1.08-1.22	<0.01
Family History of DM	1.40	1.12-1.76	<0.01
Physical Activity	0.85	0.72-1.01	0.07
Healthy Dietary Habits	0.78	0.65-0.94	0.01
History of GDM	1.50	1.20-1.87	<0.01
Presence of NAFLD	1.65	1.30-2.10	<0.01

Discussion

The study aimed to examine the incidence of prediabetes and diabetes in females with a history of GDM and NAFLD. A total of 200 participants were allotted into four groups: Group A (GDM only), Group B (NAFLD only), Group C (both GDM and NAFLD), and Group D (control group with neither condition).

Over a two-year follow-up period, the highest incidence of prediabetes and diabetes was observed in Group C, with 60% developing prediabetes and 50% developing diabetes. Group A had a prediabetes incidence of 40% and a diabetes incidence of 20%. Group B showed a prediabetes incidence of 36% and a diabetes incidence of 24%. The control group (Group D) had the lowest incidence,

with 20% developing prediabetes and 10% developing diabetes. These differences were statistically significant, representing a strong relationship between the combined history of GDM and NAFLD and the development of prediabetes and diabetes.

Significant risk factors identified through Cox proportional hazards models included higher BMI, family history of diabetes, history of GDM, and presence of NAFLD. Conversely, healthy dietary habits were found to be protective against the development of these conditions. Physical activity showed a trend towards a protective effect but was not statistically significant.

The results highlight a critical finding: females with both a history of GDM and NAFLD (Group C) are at a significantly higher risk of developing prediabetes and diabetes compared to those with only one or neither condition. This underscores the synergistic effect of GDM and NAFLD in increasing metabolic risk.

Women with both GDM and NAFLD are the most vulnerable to developing prediabetes and diabetes, as evidenced by the highest incidence rates in this group. This suggests that there is a compounded effect of these two conditions, making these women particularly high-risk and necessitating closer monitoring and preventive measures.

The study also identified higher BMI, family history of diabetes, GDM, and NAFLD as independent risk factors for the development of prediabetes and diabetes. These factors should be closely monitored in clinical practice to classify people at high risk. On the other hand, healthy dietary habits were shown to have a protective effect, indicating that lifestyle modifications can play a crucial role in preventing the progression to prediabetes and diabetes.

Clinically, these findings emphasize the need for targeted interventions for females with a history of both GDM and NAFLD. Healthcare providers should prioritize this

group for early interventions, including lifestyle modifications and possibly pharmacological treatments, to prevent the onset of prediabetes and diabetes. Regular screening for glucose intolerance in females with a history of GDM and/or NAFLD is essential to detect early signs of these metabolic conditions. Moreover, promoting healthy dietary habits and weight management can significantly reduce the risk of developing prediabetes and diabetes.

Liver fat development is more common in women with a history of GDM. According to a study, these women had higher rates of liver fat ($p=0.009$), as did those who went on to acquire pre-diabetes or diabetes ($p=0.0003$). Severe liver fat was associated with higher fasting and 2-hour glucose levels, as well as poorer insulin sensitivity and beta-cell function (all $p<0.0001$). Moderate liver fat was associated with a threefold increase in the probability of acquiring pre-diabetes or diabetes (OR=3.66, 95% CI 1.1 to 12.5), as well as worse insulin sensitivity ($p=0.0002$) and higher 2-hour glucose ($p=0.009$) [6].

In a different study, women with a history of GDM were asked to rate the Fatty Liver Index (FLI) as a predictor of metabolic degradation. It was discovered that, in comparison to those with a low FLI (≤ 20), those with a high FLI (≥ 60) had greater levels of inflammatory markers and a greater likelihood of acquiring T2DM during a ten-year period (HR: 7.85, 95% CI 2.02–30.5, $p=0.003$) [7].

A study reported that 24% of women with previous GDM had NAFLD. These women also had higher BMI, larger waist circumferences, and greater insulin resistance ($p=0.0002$, $p=0.0003$, and $p=0.0004$, respectively). Insulin resistance and waist circumference were significant independent factors associated with NAFLD [8].

Furthermore, a study found that women who had GDM during gestation were at a

higher risk for liver complications years later. These women had increased risks of abnormal liver function scores and liver fat indices (NAFLD-LFS, FLI, HSI), with adjusted relative risks of 2.34, 1.59, and 1.44, respectively [9].

In a large cohort study, NAFLD was detected as a significant risk factor for developing insulin-requiring GDM. Females with NAFLD had a higher likelihood of requiring insulin for GDM (OR=4.19; 95% CI 3.37–5.23), with risk increasing across fatty liver index categories [10].

A study highlighted the close relationship between gestational diabetes and NAFLD. It emphasized that GDM increases the risk of developing fatty liver, which exacerbates insulin resistance and disrupts glucose metabolism, necessitating close monitoring and management [11].

Conclusion:

In conclusion, this study provides strong evidence for the need for proactive management strategies in females with a history of GDM and NAFLD to mitigate their high risk of progressing to prediabetes and diabetes. Early intervention and lifestyle modifications can be pivotal in managing and preventing these metabolic disorders in this high-risk population.

Limitations: The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Healthcare providers should prioritize monitoring and managing women with both GDM and NAFLD to prevent the onset of prediabetes and diabetes. Regular screening and promoting healthy lifestyle modifications are essential to mitigate these risks.

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List of abbreviations:

BMI: Body Mass Index
 CI: Confidence Interval
 DM: Diabetes Mellitus
 FLI: Fatty Liver Index
 GDM: Gestational Diabetes Mellitus
 HbA1c: Hemoglobin A1c
 HR: Hazard Ratio
 NAFLD: Non-Alcoholic Fatty Liver Disease
 OGTT: Oral Glucose Tolerance Test
 T2DM: Type 2 Diabetes Mellitus

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