**Student's Journal of Health Research Africa**
**e-ISSN: 2709-9997, p-ISSN: 3006-1059**
**Vol. 5 No. 6 (2024): June 2024 Issue**
**https://doi.org/10.51168/sjhrafrica.v5i6.1269**
**Original Article**

# INCIDENCE OF PREDIABETES AND DIABETES IN WOMEN WITH PREVIOUS GESTATIONAL DIABETES AND NON-ALCOHOLIC FATTY LIVER DISEASE: A PROSPECTIVE COHORT STUDY.

*Rajesh Ranjan Behera[a*], Manisha Kumari[b]*
*[a]Consultant, Department of General Medicine, Kalinga Institute of Medical Sciences (KIIMS), India.*
*[b]Senior Resident, Department of Obstetrics & Gynaecology, IMS & SUM Hospital, India.*



## ABSTRACT

### Background

Non-alcoholic fatty liver disease (NAFLD) and gestational diabetes mellitus (GDM) are two common metabolic disorders that have similar pathophysiological mechanisms, including chronic inflammation and resistance to insulin. The aim of this research was to examine the incidence of prediabetes and diabetes in females who had previously experienced GDM and NAFLD, and to determine the variables linked to the advancement of glycaemic categories within this cohort.

### Methods

The study included 230 women who were evaluated for NAFLD at a baseline postpartum visit. The participants were categorized based on their GDM status during pregnancy and NAFLD presence. Incidence rates of prediabetes and diabetes were calculated, and significant predictors of glycaemic progression were identified. Data collection included medical history, anthropometric measurements, and biochemical parameters. Statistical analyses were performed using Stata 15.0.

### Results

Of 230 women, 167 (72.6%) had GDM, and 63 (27.4%) had normoglycaemia during pregnancy. Over 3 years, 98 (42.6%) developed prediabetes or diabetes, with higher incidence rates in those with both GDM and NAFLD. Key factors for glycaemic progression were age >35 (OR 2.3, p=0.005), postpartum overweight/obesity (OR 3.1, p<0.001), family history of diabetes (OR 1.9, p=0.02), and NAFLD presence (OR 2.7, p=0.001). Cardiometabolic risk factors worsened significantly, especially in women with GDM and NAFLD.

### Conclusion

Females with GDM and NAFLD are at high risk for prediabetes and diabetes. Glycaemic progression is predicted by age, postpartum BMI, family history of diabetes, and NAFLD. These findings suggest targeted surveillance and early intervention to avoid diabetes and manage cardiometabolic hazards in this high-risk group.

### Recommendations

Regular screening for glycaemic status and cardiometabolic risk factors should be prioritized in females with a history of GDM and NAFLD. Lifestyle interventions focusing on weight management and metabolic health are essential to reduce the progression to prediabetes and diabetes in this high-risk group.

***Keywords**: Non-Alcoholic Fatty Liver Disease, Gestational Diabetes Mellitus, Prediabetes, Type 2 Diabetes Mellitus, Glycaemic Progression*
*Submitted: 2024-05-15 Accepted: 2024-06-28*

***Corresponding Author:** Rajesh Ranjan Behera,*
*Email: ranjanrajesh12470@gmail.com*
*Consultant, Department of General Medicine, Kalinga institute of medical sciences (KIIMS), India.*

## INTRODUCTION

One common pregnancy problem is gestational diabetes mellitus (GDM), which is characterised by glucose intolerance that begins or is first detected during pregnancy. Approximately 7% of pregnancies globally are affected by it, with variations based on the population investigated and the diagnostic criteria employed [1]. Type 2 diabetes mellitus (T2DM) and other metabolic problems are more likely to strike women with a record of GDM later in life. The higher risk is caused by pathophysiological mechanisms such as chronic insulin resistance and β-cell dysfunction, which continue even after the pregnancy-related GDM resolves [2].

Another common metabolic disorder is non-alcoholic fatty liver disease (NAFLD), which is defined by the buildup of fat in the liver without a substantial alcohol intake. It is linked to obesity, insulin resistance, and dyslipidemia and is observed as the hepatic manifestation of metabolic syndrome. Independent of other metabolic risk factors, NAFLD is becoming more widely acknowledged as a substantial risk factor for the development of T2DM [3].

**Student's Journal of Health Research Africa**
**e-ISSN: 2709-9997, p-ISSN: 3006-1059**
**Vol. 5 No. 6 (2024): June 2024 Issue**
**https://doi.org/10.51168/sjhrafrica.v5i6.1269**
**Original Article**



Co-occurring NAFLD and GDM is an especially high-risk metabolic profile. The pathophysiological mechanisms common to both illnesses include insulin resistance and chronic inflammation, which together raise the risk of developing T2DM [4]. According to earlier research, women with NAFLD and a history of GDM have a significantly increased chance of developing T2DM as opposed to those without NAFLD [5].

Though there is established evidence linking GDM, NAFLD, and the ensuing risk of T2DM, there are few long-term studies investigating the prevalence of prediabetes and diabetes in this high-risk population. To prevent postpartum women from acquiring diabetes, it is essential to comprehend these factors and design tailored screening and intervention techniques.

The aim of this research was to examine the incidence of prediabetes and diabetes in females who had previously experienced GDM and NAFLD, and to determine the variables linked to the advancement of glycaemic categories within this cohort.

## METHODOLOGY

### Study Design

A prospective cohort observational study.

### Study Setting

The study was carried out at a tertiary care centre from November 2020 to April 2024.

### Participants

The study included 230 women.

### Inclusion criteria

- Women evaluated for NAFLD status at the baseline postpartum visit.
- Women who had GDM or normal glucose levels during their index pregnancy as per IADPSG criteria.
- At least six months post-partum at the time of baseline evaluation.

### Exclusion Criteria

- Women who had hyperglycemia throughout their index pregnancy that wasn't caused by GDM, such as overt or pre-existing diabetes.
- Females who at the time of study evaluation had diabetes or were expecting.
- Women who, in the previous year, had a hepatitis B or C infection, used a large amount of alcohol (>14 drinks per week), or used steroids (apart from foetal lung maturation during pregnancy).
- A record of severe organ damage, persistent infections, connective tissue diseases, persistent inflammatory illnesses, or usage of other medications known to induce hepatic steatosis.

### 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

### Recruitment of Participants and Testing Day Procedures

The centre invited participants to come in fasting (minimum of 10 hours fast). Anthropometric and biochemical parameter assessments were carried out, and medical histories were recorded. There was a detailed description of the anthropometric procedures, sample collection, transportation, and analysis procedures, and the procedures for the oral glucose tolerance test (OGTT).

### Diagnosis of NAFLD

After a 10-hour fast, all subjects had abdominal ultrasonography (USG) utilising a curvilinear probe (2–5 MHz) on a Supersonic Aixplorer Imagine USG equipment. The scans were carried out by two consultant radiologists who were blind to the clinical information of the individuals. During the baseline postpartum visit, NAFLD was identified using a conventional procedure. The following was used to grade the severity of hepatic steatosis:

- Echogenicity is normal (grade 0).
- Grade 1: Notable periportal and diaphragmatic echogenicity but raised hepatic echogenicity.

**Student's Journal of Health Research Africa**
**e-ISSN: 2709-9997, p-ISSN: 3006-1059**
**Vol. 5 No. 6 (2024): June 2024 Issue**
**https://doi.org/10.51168/sjhrafrica.v5i6.1269**
**Original Article**



- Grade 2: Diaphragmatic echogenicity is evident, but hepatic echogenicity is increased and obscures periportal echogenicity.
- Grade 3: Periportal and diaphragmatic echogenicity are obscured by increased hepatic echogenicity.

## Bias

Bias was minimized by using standardized diagnostic criteria, ensuring radiologists were blinded to clinical data, and excluding participants with conditions that could confound the study results.

## Variables

The primary variables included the incidence of prediabetes and diabetes, NAFLD status, GDM status, age, postpartum BMI, and family record of diabetes.

## Data Collection

Data collection involved recording medical history, anthropometric measurements, and biochemical parameters. Standardized procedures were followed to ensure data accuracy and reliability.

## Statistical Analysis

Stata 15.0 was used for the statistical analysis. Numbers (%), means ± standard deviations, or medians, if applicable, were used to present the data. For each group, the prevalence rates of prediabetes and diabetes per 100 woman-years were computed. The odds ratios were used to express the results. In the logistic regression analysis, the dichotomous variables of age >35 and weight gain >5% were employed. We computed and analysed changes in cardiometabolic risk variables across various categories between visits. The reference group consisted of pregnant women without NAFLD who did not have normoglycemia. There was a significance threshold of $P < 0.05$.

## Ethical considerations

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

## RESULT

Out of the 230 women included in the study, 167 (72.6%) had a history of GDM, while 63 (27.4%) had normoglycaemia during pregnancy. The baseline characteristics of the participants, including age, BMI, family record of diabetes, and presence of NAFLD, are detailed in Table 1.

During the median follow-up period of 3 years, 98 (42.6%) women developed prediabetes or diabetes. The incidence rates per 100 woman-years were considerably higher in females with a history of GDM and NAFLD in contrast to those without NAFLD or with normoglycaemia during pregnancy (Table 2).

Several characteristics were found to be substantially linked with the transition from normoglycemia to prediabetes or diabetes by multivariate logistic regression analysis (Table 3).

Significant differences were observed in cardiometabolic risk factors relating the baseline and follow-up visits. Females with GDM and NAFLD showed the most substantial changes in these parameters (Table 4).

A further breakdown of glycaemic progression rates showed that females with both GDM and NAFLD had the highest rates of developing prediabetes or diabetes. The adjusted hazard ratios (HRs) indicated that these women were significantly more likely to experience glycaemic progression compared to other groups (Table 5)

**Table 1: Participant Characteristics**

| Characteristic | GDM (n=167) | Normoglycaemia (n=63) | p-value |
|---|---|---|---|
| Age (years) | 32.4 ± 4.5 | 31.8 ± 4.1 | 0.35 |
| BMI (kg/m²) | 28.7 ± 3.2 | 25.6 ± 2.9 | <0.001 |
| Family history of diabetes (%) | 92 (55.1%) | 20 (31.7%) | 0.002 |
| NAFLD presence (%) | 103 (61.7%) | 18 (28.6%) | <0.001 |

**Table 2: Incidence of Prediabetes and Diabetes**

| Group | Incidence Rate per 100 Woman-Years | HR (95% CI) | Adjusted HR (95% CI) |
|---|---|---|---|
| GDM + NAFLD (n=103) | 14.2 (11.8–17.2) | 3.4 (2.1–5.4) | 2.8 (1.7–4.6) |
| GDM + No NAFLD (n=64) | 8.9 (6.3–12.4) | 2.2 (1.3–3.7) | 2.0 (1.2–3.4) |
| Normoglycaemia + NAFLD (n=18) | 5.1 (2.6–9.8) | 1.4 (0.7–2.8) | 1.2 (0.6–2.5) |
| Normoglycaemia + No NAFLD (n=45) | 3.7 (2.1–6.4) | 1.0 (Reference) | 1.0 (Reference) |

**Student's Journal of Health Research Africa**
**e-ISSN: 2709-9997, p-ISSN: 3006-1059**
**Vol. 5 No. 6 (2024): June 2024 Issue**
**https://doi.org/10.51168/sjhrafrica.v5i6.1269**
**Original Article**



**Table 3: Factors Associated with Glycaemic Progression**

| Variable | OR (95% CI) | p-value |
|---|---|---|
| Age >35 years | 2.3 (1.3–4.1) | 0.005 |
| Postpartum BMI (overweight/obesity) | 3.1 (1.8–5.4) | <0.001 |
| Family history of diabetes | 1.9 (1.1–3.4) | 0.02 |
| NAFLD presence | 2.7 (1.5–4.9) | 0.001 |

**Table 4: Changes in Cardiometabolic Risk Factors**

| Parameter | Baseline | Follow-up | Change (%) | p-value |
|---|---|---|---|---|
| Fasting glucose (mg/dL) | 98.2 ± 12.3 | 108.7 ± 14.6 | +10.7% | <0.001 |
| HbA1c (%) | 5.6 ± 0.4 | 5.9 ± 0.6 | +5.4% | <0.001 |
| Triglycerides (mg/dL) | 135.4 ± 45.7 | 149.3 ± 50.1 | +10.2% | 0.03 |
| HDL cholesterol (mg/dL) | 45.2 ± 8.1 | 42.7 ± 7.6 | -5.5% | 0.02 |
| Systolic blood pressure (mmHg) | 122.6 ± 14.3 | 127.8 ± 15.1 | +4.2% | 0.01 |

**Table 5: Detailed Analysis of Glycaemic Progression**

| Group | Number of Progressions (%) | Adjusted HR (95% CI) | p-value |
|---|---|---|---|
| GDM + NAFLD (n=103) | 58 (56.3%) | 2.8 (1.7–4.6) | <0.001 |
| GDM + No NAFLD (n=64) | 25 (39.1%) | 2.0 (1.2–3.4) | 0.004 |
| Normoglycaemia + NAFLD (n=18) | 10 (55.6%) | 1.2 (0.6–2.5) | 0.27 |
| Normoglycaemia + No NAFLD (n=45) | 5 (11.1%) | 0.1 (Reference) | - |

## DISCUSSION

The study included 230 women, divided into two groups: 167 with a history of GDM and 63 with normoglycaemia during pregnancy. Women with GDM had significantly higher BMI and a greater prevalence of NAFLD compared to those with normoglycaemia.

Over a median follow-up of 3 years, 42.6% of the participants developed prediabetes or diabetes. The incidence was notably higher in females with both a history of GDM and NAFLD. Specifically, the incidence rate per 100 woman-years was 14.2 for the GDM + NAFLD group, compared to only 3.7 for the normoglycaemia + No NAFLD group. The adjusted hazard ratios confirmed that having both GDM and NAFLD significantly increased the risk of developing prediabetes or diabetes.

Multivariate analysis identified key factors associated with the progression to prediabetes or diabetes. Age over 35 years, postpartum overweight/obesity, family record of diabetes, and the presence of NAFLD were all significant predictors of glycaemic progression. These findings suggest that these factors should be closely monitored in postpartum women to identify those at higher risk.

Women with GDM and NAFLD exhibited significant changes in cardiometabolic risk factors over the study period. They showed increases in fasting glucose, HbA1c, triglycerides, and systolic blood pressure, along with a decrease in HDL cholesterol. These changes indicate a deterioration in metabolic health, further emphasizing the increased risk for this group.

The results of this study highlight the compounded risk of developing prediabetes and diabetes in females with a record of GDM and NAFLD. The significant predictors identified—age over 35, postpartum overweight/obesity, family history of diabetes, and NAFLD presence—suggest that targeted interventions are necessary for these high-risk groups.

Women with both GDM and NAFLD have worsening cardiometabolic risk factors, which suggests a higher risk of metabolic syndrome and cardiovascular illnesses. To reduce this risk, comprehensive management techniques are required.

Overall, the study underscores the critical need for early and proactive monitoring of females with a record of GDM and NAFLD to prevent the progression to prediabetes and diabetes and to manage associated cardiometabolic risks effectively.

Recent studies have shed light on the complex relationship between GDM and NAFLD, highlighting their combined impact on metabolic health and the risk of developing T2DM. A study explored the genetic interplay between NAFLD and GDM, using genome-wide association studies (GWAS) data. The study revealed a potential bidirectional relationship, suggesting that genetic predisposition to NAFLD might influence the risk of

developing GDM, and vice versa. The study used the inverse variance weighted (IVW) method and found significant associations, reinforcing the need to consider genetic factors in understanding the risk of these conditions [6].

Researchers looked into the relationships between the risk of GDM and liver enzymes and the hepatic steatosis index (HSI) in a prospective study involving pregnant Chinese women. Using ultrahigh-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS), 948 plasma samples were examined for the investigation. Higher concentrations of particular lipid metabolites and liver biomarkers were found to be strongly linked to a higher risk of GDM. Higher quartiles of liver biomarkers were associated with higher odds ratios (ORs) for GDM, suggesting a possible role for these biomarkers as early predictors of GDM [7].

The interaction between haemoglobin (Hb) concentration in the first trimester and NAFLD during pregnancy was investigated in a different study. This study, which involved a cohort of pregnant Chinese women, discovered that the risk of GDM was considerably enhanced when raised Hb levels were paired with NAFLD. Women with high Hb levels and NAFLD had significantly greater odds of developing GDM, highlighting the need of taking into account several biomarkers in GDM risk assessment [8].

Research assessed the impact of NAFLD on the risk of incident diabetes. The study concluded that NAFLD independently increased the risk of developing T2DM, with a significant hazard ratio (HR) even after adjusting for other metabolic risk factors. This finding underscores the critical role of liver health in diabetes prevention and management [6, 9].

### Generalizability

The study "Incidence of Prediabetes and Diabetes in Women with Previous Gestational Diabetes and Non-Alcoholic Fatty Liver Disease: A Prospective Study" reveals that women with both GDM and NAFLD are at significantly higher risk for developing prediabetes and diabetes. Key predictors of glycaemic progression include age over 35, postpartum BMI, family history of diabetes, and the presence of NAFLD. These findings suggest that targeted monitoring and early interventions for women with these risk factors are essential. The study's comprehensive approach and significant sample size support the applicability of its results to a broader population, indicating similar trends could be expected in larger or different cohorts.

## CONCLUSION

The study demonstrates that females with a record of GDM and NAFLD are at a significantly greater risk of developing prediabetes and diabetes postpartum. Key risk factors identified include age over 35, postpartum overweight/obesity, family record of diabetes, and the presence of NAFLD. These findings highlight the necessity for targeted monitoring and early intervention strategies in this high-risk population to prevent glycaemic progression and manage cardiometabolic risks effectively.

## 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

Regular screening for glycaemic status and cardiometabolic risk factors should be prioritized in females with a history of GDM and NAFLD. Lifestyle interventions focusing on weight management and metabolic health are essential to reduce the progression to prediabetes and diabetes in this high-risk group.

## ACKNOWLEDGEMENT

We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staff of our hospital who were involved in patient care of the study group.

## LIST OF ABBREVIATIONS

NAFLD: Non-Alcoholic Fatty Liver Disease
GDM: Gestational Diabetes Mellitus
BMI: Body Mass Index
T2DM: Type 2 Diabetes Mellitus
OGTT: Oral Glucose Tolerance Test
USG: Ultrasonography
IADPSG: International Association of Diabetes and Pregnancy Study Groups
HR: Hazard Ratio
CI: Confidence Interval
OR: Odds Ratio
IVW: Inverse Variance Weighted
UHPLC-MS: Ultrahigh-Performance Liquid Chromatography-Tandem Mass Spectrometry
Hb: Hemoglobin
HSI: Hepatic Steatosis Index

## SOURCE OF FUNDING

No funding received.

## CONFLICT OF INTEREST

The authors have no conflicting interests to declare.

## REFERENCES



1. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020. Diabetes Care. 2020;43(Suppl 1):S14-S31.
2. Zhu Y, Zhang C. Prevalence of Gestational Diabetes and Risk of Progression to Type 2 Diabetes: A Global Perspective. Curr Diab Rep. 2016;16(1):7.
3. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328-357.
4. Bril F, Cusi K. Nonalcoholic fatty liver disease: the new complication of type 2 diabetes mellitus. Endocrinol Metab Clin North Am. 2016;45(4):765-781.
5. Shah, A., & Campos, A. P. (2017). Gestational Diabetes and the Risk of Developing Type 2 Diabetes: A Systematic Review. Journal of Women's Health, Issues & Care, 6(3), 1000326.
6. Liu X, Li Y, Wang M, et al. Non-alcoholic fatty liver disease and gestational diabetes mellitus: a bidirectional two-sample mendelian randomization study. BMC Endocr Disord. 2022;22:41.
7. Wang L, Xie W, Yan J, et al. Liver biomarkers, lipid metabolites, and risk of gestational diabetes mellitus in a prospective study among Chinese pregnant women. BMC Med. 2022;20:282.
8. Zhang Y, Ma X, Wu C, et al. The interactive effects of non-alcoholic fatty liver disease and hemoglobin concentration in the first trimester on the development of gestational diabetes mellitus. PLoS One. 2022;17(3):e0248663.
9. Targher G, Day CP, Bonora E. Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. N Engl J Med. 2010;363(14):1341-1350.

## PUBLISHER DETAILS

**SJC PUBLISHERS COMPANY LIMITED**

SJC Publishers Company Limited
TODAY AND TOMORROW

Catergory: Non Government & Non profit Organisation
Contact: +256 775 434 261 (WhatsApp)
Email:info@sjpublisher.org or studentsjournal2020@gmail.com
Website: https://sjpublisher.org
Location: Scholar's Summit Nakigalala, P. O. Box 701432,Entebbe Uganda, East Africa