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Relationship between breastfeeding and hepatic steatosis in women with previous gestational diabetes mellitus

Supatsri Sethasine[1] and Chadakarn Phaloprakarn[2*]

Abstract

Background Non-alcoholic fatty liver disease (NAFLD), characterized by excess liver fat, is common in women with a history of gestational diabetes mellitus (GDM). While breastfeeding improves postpartum lipid levels, its impact on NAFLD in these women is not well studied. We aimed to investigate the relationship between the duration and intensity of breastfeeding and the amount of liver fat and prevalence of NAFLD in women with previous GDM at approximately 1 year postpartum.

Methods This prospective cohort study was conducted at a university hospital in Bangkok, Thailand between November 2021 and February 2024. Overall, 130 women who had experienced GDM in their most recent pregnancy were followed up for 1 year postpartum. We collected data on breastfeeding practices and quantified liver fat using controlled attenuation parameters (CAPs) during transient elastography. NAFLD was defined as a CAP of ≥ 302 dB/m. Women were divided into three groups according to the duration and intensity of breastfeeding: group 1 (breastfeeding for < 6 months), group 2 (breastfeeding for ≥ 6 months and exclusive breastfeeding [EBF] for < 6 months), and group 3 (breastfeeding for ≥ 6 months and EBF for 6 months).

Results Overall, 57 (43.8%), 26 (20.0%), and 47 (36.2%) participants were categorized into groups 1, 2, and 3, respectively. Group 3 had the lowest CAPs, followed by groups 2 and 1. The median values (interquartile ranges) of the CAPs were 219.0 (189.0–271.0) dB/m, 257.5 (205.3–317.3) dB/m, and 279.0 (191.5–324.0) dB/m for groups 3, 2, and 1, respectively ($p = 0.034$). NAFLD prevalence was significantly lower in group 3 compared to groups 2 and 1 (19.1% vs. 38.5% vs. 43.9%, respectively; $p = 0.026$). Multivariate analysis showed that breastfeeding for ≥ 6 months and EBF for 6 months reduced the risk of NAFLD, with an adjusted odds ratio of 0.34 (95% confidence interval 0.14, 0.95).

Conclusions Breastfeeding for ≥ 6 months, particularly EBF for the first 6 months, may offer a practical strategy to reduce the risk of NAFLD in women with prior GDM.

Trial registration Thai Clinical Trials Registry: Registration no. TCTR20211027008. Date of registration: October 27, 2021. Date of initial participant enrollment: November 1, 2021.

Keywords Breastfeeding, Fatty liver, Gestational diabetes mellitus, Hepatic steatosis, Lactation, Non-alcoholic fatty liver disease

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Background

The global prevalence of gestational diabetes mellitus (GDM) has been on the rise recently [1]. This increase aligns with the increasing prevalence of obesity, especially in women of reproductive age [2]. Women with a history of GDM have a higher risk of future type 2 diabetes mellitus and metabolic syndrome (MetS) [3, 4] and are also at an increased risk of developing non-alcoholic fatty liver disease (NAFLD) compared with those who have not experienced GDM [5–7].

NAFLD is characterized by the accumulation of excessive fat in the liver. NAFLD is considered benign; however, it can progress to liver cirrhosis and hepatocellular carcinoma [8, 9]. Moreover, NAFLD is recognized as a risk factor for atherosclerotic cardiovascular disease, which is a leading cause of death globally [10]. Therefore, the prevention of NAFLD is crucial before the development of disease-related complications.

Breastfeeding improves postpartum glucose and lipid metabolism in women with a history of GDM [11–15]. NAFLD is a well-recognized hepatic manifestation of metabolic disorder. However, no study has directly investigated the protective role of breastfeeding against NAFLD in women with previous GDM. Furthermore, only two studies have explored the relationship between breastfeeding duration and the prevalence of NAFLD in parous women from a general population [16, 17].

The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) advocate exclusive breastfeeding (EBF) for the first 6 months of a baby's life, followed by complementary feeding and continued breastfeeding for approximately 2 years or beyond [18]. The emphasis on the intensity (EBF for the first 6 months) and duration (approximately 2 years or beyond) of breastfeeding is based on the understanding that this approach can maximize health benefits for the mother and child. Evidence suggests that a longer breastfeeding duration is associated with a reduced risk of NAFLD. However, the effect of combining a longer duration and higher intensity of breastfeeding, as recommended by the WHO and UNICEF, on hepatic steatosis remains unclear.

This study aimed to investigate the association between the duration and intensity of breastfeeding and the amount of liver fat and NAFLD prevalence in women with previous GDM 1 year postpartum.

Methods

Study design, setting, and population

The Fatty Liver Disease after Gestational Diabetes Mellitus (FLD-GDM) study was an umbrella project exploring various aspects of hepatic steatosis in women with a history of GDM. Conducted between November 2021 and February 2024 at a university hospital in Bangkok, Thailand, the study followed women for approximately 1 year postpartum after a GDM pregnancy. It served as a prospective observational extension of earlier research on breastfeeding and postpartum weight changes and their effects on metabolic health at 6 months postpartum [15, 19].

This sub-project of the FLD-GDM study specifically examined the relationship between breastfeeding, liver fat accumulation, and NAFLD prevalence. The study protocol was approved by the Institutional Review Board (certificate no. 117/2564) and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Participants were required to have been part of earlier studies on breastfeeding and postpartum weight changes [15, 19]. The exclusion criteria included current pregnancy, alcohol consumption, hepatitis B or C viral infections, receiving medications associated with hepatic steatosis, such as corticosteroids, amiodarone, valproate, tamoxifen, and methotrexate, and refusal to participate.

For earlier studies, the inclusion criteria were: (1) age ≥ 18 years; (2) having antenatal care and GDM screening at the hospital; and (3) being diagnosed with GDM based on the Carpenter and Coustan criteria [20]. Exclusion criteria included HIV infection, pregnancy during the study period, use of contraindicated medications during breastfeeding, and loss during follow-up.

Sample size

The sample size was calculated based on findings from a previous study indicating a 62.7% prevalence of NAFLD in women with a history of GDM [7]. To detect a 54% reduction in NAFLD prevalence among women who breastfed for ≥6 months [16] (from 62.7 to 28.8%) with 80% power at a two-sided significance level of 0.05, a minimum of 99 participants was required. These participants were divided into three groups: 33 women who breastfed for <6 months, 33 who breastfed for ≥6 months and exclusively breastfed for <6 months, and 33 who breastfed for ≥6 months and exclusively breastfed for 6 months. This study is a prospective observational extension of previous studies that examined the effects of breastfeeding and postpartum weight changes on metabolic health at 6 months postpartum in women with prior GDM [15, 19]. Consequently, the present study included all women who participated in these earlier studies.

Participant recruitment

Potential participants were approached when presenting for follow-up 6 months postpartum in earlier studies [15, 19] or while attending the gynecology outpatient clinic for an annual Pap test 1 year after delivery. Participants were informed about the FLD-GDM study. All participants provided written informed consent before participating in the study.

Eligible participants were scheduled for blood tests and liver fat quantification at approximately 1 year postpartum, within a time frame of 15 months after delivery. They were instructed to refrain from eating or drinking anything 12 h before their scheduled appointment.

Procedure

On the scheduled date, participants were interviewed about their breastfeeding practices. They were asked about the duration of breastfeeding, the time at which they stopped breastfeeding or expressed milk, and the time they introduced formula or foods/drinks. Furthermore, feeding practice data were obtained from records in a mini calendar provided to the participants and the hospital's electronic database during the baby's routine follow-up visits [15]. A specially trained nurse performed a physical examination, measuring height, weight, blood pressure, and waist circumference (WC), as detailed in a previous publication [19].

After the physical examination, venous blood samples were drawn for fasting plasma glucose (FPG), glycated hemoglobin (hemoglobin A1c), insulin, and C-peptide; lipid analyses including cholesterol, triglycerides (TG), low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol (HDL-C); and liver function tests including aspartate aminotransferase, alanine transaminase, and alkaline phosphatase. All blood samples were collected after a 12-h overnight fast. FPG, hemoglobin A1c, and lipid measurements were performed using standard techniques as previously described [19]. Fasting insulin and C-peptide levels were analyzed with a Cobas e801 (Roche Diagnostics, Mannheim, Germany). Liver function tests were performed using a Cobas c503 analyzer (Roche Diagnostics). The homeostasis model assessment of insulin resistance was calculated using the following formula: fasting glucose (mg/dL) x fasting insulin (μU/mL) / 405 [21]. Prediabetes was defined as FPG ≥ 100 mg/dL [22], and MetS was diagnosed following the joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention [23].

Liver fat was measured using the controlled attenuation parameter (CAP) via the transient elastography model FibroScan® 502 Touch (Echosens, Paris, France), with liver stiffness measurements (LSMs) conducted simultaneously. All examinations were performed by a single experienced hepatologist blinded to participants' clinical data, using either a 3.5 MHz M probe or a 2.5 MHz XL probe, depending on the participant. Measurements were taken on the right lobe of the liver through the intercostal spaces, with the participants lying supine with the right arm in abduction. The success rate was calculated as the number of successful measurements divided by the total number of measurements. The median values of successful CAP and LSM measurements were reported in decibels per meter (dB/m) and kilopascal (kPa), respectively. Reliable measurements required ≥ 10 valid measurements, a success rate of ≥ 60%, a CAP interquartile range (IQR) < 40 dB/m, and an LSM IQR/median ratio < 0.3. Only measurements meeting these criteria were included in the analysis.

Data collection and outcome measures

Data collection included baseline characteristics at 6 weeks postpartum and clinical data at approximately 1 year after delivery. Baseline characteristics were drawn from earlier studies [15, 19], while 1-year data included breastfeeding practices, contraception methods, body mass index (BMI), blood pressure, WC, laboratory results, CAP value, LSM, and NAFLD status. Due to the lack of a standardized CAP threshold for detecting steatosis in this population, we used a cutoff of 302 dB/m, as identified in a prior study on adults suspected of NAFLD [24].

The participants were divided into three groups based on the duration and intensity of the breastfeeding: group 1 (breastfeeding for < 6 months), group 2 (breastfeeding for ≥ 6 months and EBF for < 6 months), and group 3 (breastfeeding for ≥ 6 months and EBF for 6 months). EBF was defined as feeding only breast milk without additional foods or liquids [25], with the duration assessed from birth to six months postpartum. The outcome measures were liver fat content and NAFLD prevalence.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corporation, Armonk, NY, USA). Chi-squared or Fisher's exact tests, as appropriate, were performed to compare categorical variables. The means of continuous variables between the three breastfeeding practice groups were compared using a one-way analysis of variance. When the overall comparison showed significant differences, intergroup comparisons were performed using the least significant difference method as a post hoc test. Differences in the medians of continuous variables among the three groups were analyzed using the Kruskal–Wallis H test, followed by the Dunn-Bonferroni post hoc test for pairwise comparisons.

Changes in the means of variables over time (between baseline and 1 year postpartum) within each group were analyzed using paired t-tests. Differences in these changes between the three groups were examined using a one-way analysis of covariance, controlling for the baseline value of each parameter. Changes in the prevalence rates of prediabetes and MetS within each group over time were calculated using McNemar's test, while differences in these changes between the three groups were compared using the chi-squared test. To assess the

relationship between breastfeeding and NAFLD, multivariate logistic regression analysis was performed after adjusting for an a priori set of confounding variables: age, severity of GDM, method of contraception used, baseline BMI, and FPG [16, 17, 26]. Adjusted odds ratios (ORs) were estimated with 95% confidence intervals (CIs). All tests were two-sided and statistical significance was set at $p<0.05$.

Results

Among the 171 women who participated in earlier studies examining metabolic health 6 months after experiencing a GDM pregnancy, five became pregnant, six had hepatitis B viral infection, and 30 refused to participate in the present study. Therefore, 130 women were included in the final analysis. A study flow diagram, following the STROBE statement, is presented in Fig. 1.

The mean age of the 130 enrolled participants was 32.9±5.9 years. Fifty-seven participants (43.8%) were categorized into group 1, whereas 26 (20.0%) and 47 (36.2%) were categorized into groups 2 and 3, respectively. The baseline characteristics of the participants in the breastfeeding practice groups are summarized in Table 1. Group 3 had significantly lower weight, BMI, FPG and TG levels, but a significantly higher HDL-C level than group 1. Moreover, group 3 had higher HDL-C levels than group 2, with no significant differences between groups 1 and 2.

At approximately 1 year postpartum, group 3 had significantly lower weight, BMI, systolic BP, WC, FPG, fasting insulin, C-peptide, homeostasis model assessment of insulin resistance, and TG levels, but a significantly higher HDL-C level than the other two groups (Table 2). Changes in weight, BMI, FPG, and lipid levels between baseline and 1 year postpartum were not significantly different among the groups (Table 3). However, group 3 had a significantly smaller increase in the prevalence of MetS compared to the other two groups and a smaller increase in prediabetes compared to group 2.

The results of transient elastography showed that group 3 had the lowest CAP values, followed by groups 2 and 1 (Table 2). The medians (IQR) of CAP values were 219.0 (189.0–271.0) dB/m, 257.5 (205.3–317.3) dB/m, and 279.0 (191.5–324.0) dB/m for groups 3, 2, and 1, respectively; $p=0.034$.

Notably, 44 (33.8%) of the 130 participants developed NAFLD at 1 year postpartum. Figure 2 shows the prevalence of NAFLD across different breastfeeding practice

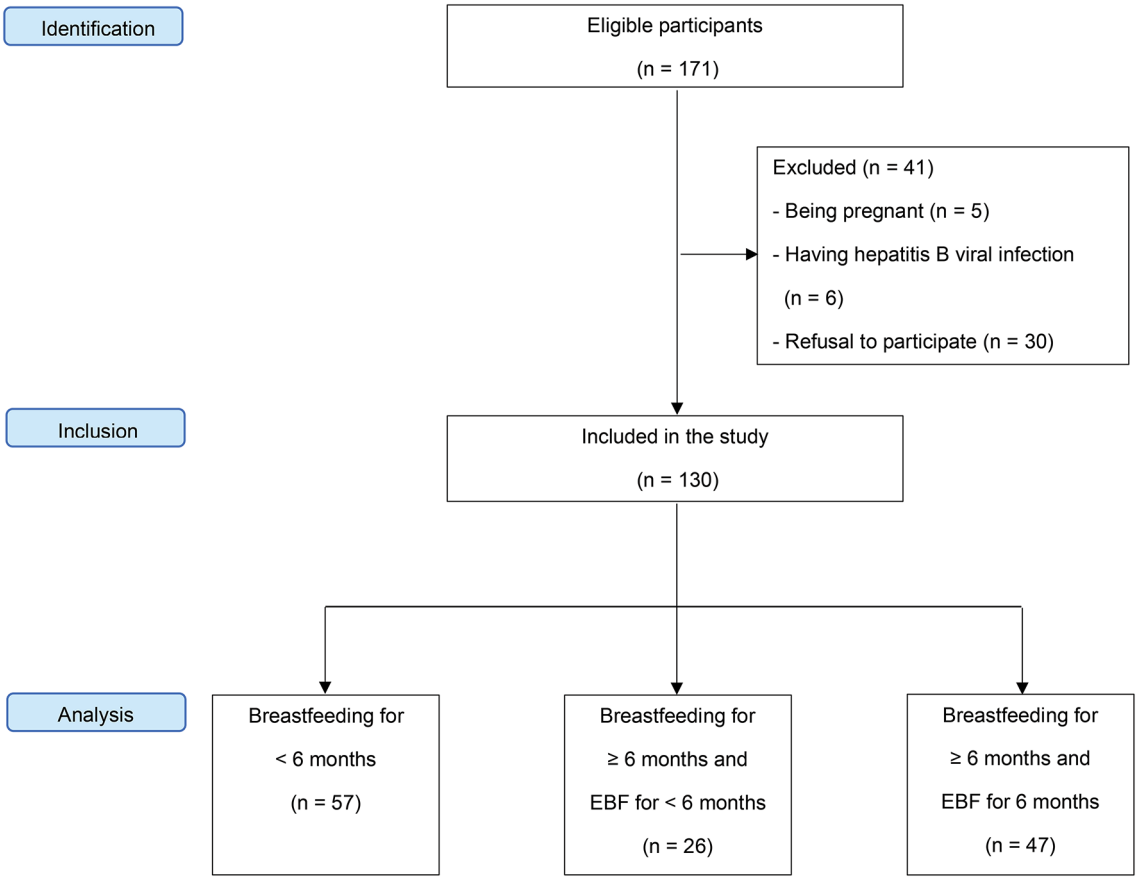

Fig. 1 STROBE flow chart. *Abbreviations: EBF* exclusive breastfeeding, *STROBE* Strengthening the Reporting of Observational Studies in Epidemiology

Table 1 Baseline characteristics of participants based on breastfeeding practice groups

	Breastfeeding practice group[a]			*p*-value[b]
	Group 1	Group 2	Group 3	
	(*n* = 57)	(*n* = 26)	(*n* = 47)	
Clinical features				
Age (years)	32.0 ± 6.1	32.6 ± 7.0	34.3 ± 4.7	0.116
Parity				0.514
Primiparous	24 (42.1)	13 (50.0)	17 (36.2)	
Multiparous	33 (57.9)	13 (50.0)	30 (63.8)	
Severity of GDM				0.284
Class A1	45 (78.9)	23 (88.5)	42 (89.4)	
Class A2	12 (21.1)	3 (11.5)	5 (10.6)	
Family history of T2DM	24 (42.1)	6 (23.1)	14 (29.8)	0.180
Weight (kg)	67.9 (55.8–76.4)	65.2 (57.4–72.6)	58.8 (52.7–66.2)[c]	0.027
BMI (kg/m^2)	27.7 (22.6–30.3)	26.4 (23.3–30.3)	24.2 (22.1–26.3)[c]	0.036
Systolic BP (mmHg)	119.0 (110.8–133.5)	124.0 (114.8–130.3)	117.5 (109.8–122.0)	0.080
Diastolic BP (mmHg)	75.0 (68.8–84.3)	74.5 (69.0–81.3)	72.0 (64.8–77.0)	0.061
WC (cm)	85.8 ± 10.2	87.8 ± 10.6	83.2 ± 10.5	0.145
Laboratory tests				
FPG (mg/dL)	91.0 (87.0–96.8)	90.5 (86.0–96.0)	86.0 (81.0–92.5)[c]	0.008
Cholesterol (mg/dL)	210.0 (193.8–228.3)	208.0 (187.0–259.5)	220.0 (192.0–244.3)	0.540
TG (mg/dL)	136.0 (93.5–211.0)	111.0 (85.8–146.3)	82.5 (65.0–115.0)[c]	< 0.001
LDL-C (mg/dL)	141.0 (123.8–158.3)	142.5 (116.3–181.8)	147.0 (117.8–171.3)	0.569
HDL-C (mg/dL)	52.5 (48.0–60.3)	54.0 (47.5–66.0)	66.0 (58.0–78.5)[c, d]	< 0.001

Data are presented as the mean ± SD or median (IQR) or n (%)

Abbreviations: BMI body mass index, *BP* blood pressure, *EBF* exclusive breastfeeding, *FPG* fasting plasma glucose, *HDL-C* high-density lipoprotein cholesterol, *IQR* interquartile range, *LDL-C* low-density lipoprotein cholesterol, *SD* standard deviation, *TG* triglycerides, *T2DM* type 2 diabetes mellitus, *WC* waist circumference

[a] Group 1 = breastfeeding for < 6 months; group 2 = breastfeeding for ≥ 6 months and EBF for < 6 months; and group 3 = breastfeeding for ≥ 6 months and EBF for 6 months

[b] Differences between groups were compared using a one-way analysis of variance, Kruskal-Wallis H test, or chi-squared test

[c] $p < 0.05$, compared with group 1

[d] $p < 0.05$, compared with group 2

groups. In a univariate analysis, breastfeeding for ≥6 months and EBF for 6 months was negatively associated with the prevalence of NAFLD (Table 4). This association remained significant after adjusting for confounders, such as age, severity of GDM, contraception method, baseline BMI, and FPG, with an adjusted OR of 0.34 (95% CI 0.14, 0.95). Other factors linked to NAFLD included the use of a progestin-only contraceptive method (adjusted OR 4.48; 95% CI 1.45, 13.89), baseline BMI (adjusted OR 1.24; 95% CI 1.10, 1.39), and FPG (adjusted OR 1.04; 95% CI 1.01, 1.07).

Discussion

This study's primary finding was that women with a history of GDM who engaged in breastfeeding for ≥6 months combined with EBF for 6 months had lower liver fat levels and a 66% lower prevalence of NAFLD at approximately 1 year postpartum compared with those who breastfed for <6 months or did not exclusively breastfeed for 6 months.

Notably, only two studies have investigated the association of breastfeeding duration with NAFLD prevalence later in life in parous women from a general population [16, 17]. The Coronary Artery Risk Development in Young Adults (CARDIA) study found a 54% lower prevalence of NAFLD at 25 years postpartum in women who breastfed for ≥6 months compared with those who breastfed for 0–1 month [16]. Similarly, the Korean National Health and Nutrition Examination Survey (KNHANES) reported a 33% reduction in NAFLD prevalence among women who breastfed for 6 to <12 months compared with those who breastfed for <1 month [17]. Our findings align with these studies, showing that the duration and intensity of breastfeeding are crucial for improving hepatic steatosis 1 year after GDM. However, the significant association was observed only in those who completed 6 months of EBF.

The mechanisms behind the protective effect of prolonged and intensive breastfeeding on NAFLD are not yet fully understood. However, one possible explanation is that breastfeeding improves glucose and lipid metabolism [11–15], both of which are associated with the development of NAFLD [27, 28]. This hypothesis is supported by our findings, which showed a significant reduction in

Table 2 Characteristics of participants at approximately 1 year postpartum based on breastfeeding practice groups

	Breastfeeding practice group[a]			*p*-value
	Group 1	Group 2	Group 3	
	(*n* = 57)	(*n* = 26)	(*n* = 47)	
Clinical characteristics				
Duration of any breastfeeding (years)	1.1 (1.0–1.2)	1.0 (1.0–1.2)	1.0 (1.0–1.1)	0.156
Current contraceptive use				0.602
No or non-hormonal method	41 (71.9)	14 (53.8)	31 (66.0)	
Combined estrogen-progestin method	6 (10.5)	4 (15.4)	5 (10.6)	
Progestin-only method	10 (17.5)	8 (30.8)	11 (23.4)	
Weight (kg)	69.1 ± 16.2	69.0 ± 11.2	59.1 ± 9.6[c, d]	< 0.001
BMI (kg/m^2)	27.7 ± 6.0	28.0 ± 4.5	24.1 ± 3.4[c, d]	< 0.001
Systolic BP (mmHg)	119.0 (112.0–126.5)	126.0 (117.0–133.0)	114.0 (109.0–121.0)[c, d]	< 0.001
Diastolic BP (mmHg)	74.0 (67.0–82.0)	76.5 (71.0–82.3)	72.0 (66.0–79.0)	0.108
WC (cm)	90.5 ± 13.9	90.2 ± 8.7	87.8 ± 12.3[c, d]	< 0.001
Laboratory tests				
FPG (mg/dL)	100.0 (90.0–106.5)	97.5 (94.0–108.3)	93.0 (87.0–101.0)[c, d]	0.030
HbA1c (%)	5.6 (5.3–5.9)	5.6 (5.4–5.7)	5.5 (5.2–5.8)	0.675
Fasting insulin (mU/L)	11.0 (8.4–20.9)	17.1 (9.6–23.4)	8.3 (5.3–11.8)[c, d]	< 0.001
Fasting C-peptide (ng/mL)	2.4 (1.9–3.2)	2.8 (2.2–3.3)	1.8 (1.5–2.3)[c, d]	< 0.001
HOMA-IR	2.8 (1.9–5.3)	4.3 (2.4–5.7)	1.9 (1.2–2.7)[c, d]	< 0.001
Cholesterol (mg/dL)	183.0 (169.0–208.0)	197.0 (176.8–228.0)	191.0 (175.0–221.0)	0.160
TG (mg/dL)	101.0 (73.0–165.5)	97.5 (83.5–167.8)	79.0 (50.0–113.0)[c, d]	0.009
LDL-cholesterol (mg/dL)	118.0 (109.0–147.0)	141.0 (109.3–170.5)	130.0 (114.0–152.0)	0.050
HDL-cholesterol (mg/dL)	49.0 (44.5–56.0)	50.0 (41.8–58.8)	61.0 (55.0–70.0)[c, d]	< 0.001
AST (U/L)	21.0 (19.0–25.5)	22.0 (18.0–27.5)	21.0 (16.0–23.0)	0.076
ALT (U/L)	17.0 (8.0–23.5)	12.5 (8.0–22.8)	12.0 (8.0–18.0)	0.462
ALP (U/L)	74.0 (59.5–84.5)	79.5 (69.0–93.3)	81.0 (63.0–97.0)	0.235
FibroScan measurements				
CAP value (dB/m)	279.0 (191.5–324.0)	257.5 (205.3–317.3)	219.0 (189.0–271.0)[c]	0.034
Liver stiffness value (kPa)	4.4 (3.6–5.4)	4.6 (3.9–5.2)	4.4 (3.5–5.5)	0.803

Data are presented as the mean ± SD or median (IQR) or n (%)

Abbreviations: ALP alkaline phosphatase, *ALT* alanine transaminase, *AST* aspartate aminotransferase, *BMI* body mass index, *BP* blood pressure, *CAP* controlled attenuation parameter, *EBF* exclusive breastfeeding, *FPG* fasting plasma glucose, *HbA1c* hemoglobin A1c, *HDL-C* high-density lipoprotein cholesterol, *HOMA-IR* homeostasis model assessment of insulin resistance, *IQR* interquartile range, *LDL-C* low-density lipoprotein cholesterol, *SD* standard deviation, *TG* triglycerides, *WC* waist circumference

[a] Group 1 = breastfeeding for < 6 months; group 2 = breastfeeding for ≥ 6 months and EBF for < 6 months; and group 3 = breastfeeding for ≥ 6 months and EBF for 6 months

[b] Differences between groups were compared using a one-way analysis of variance, Kruskal-Wallis H test, or chi-squared test

[c] $p < 0.05$, compared with group 1

[d] $p < 0.05$, compared with group 2

the rates of prediabetes and MetS at 1 year postpartum among participants who breastfed for ≥6 months and exclusively breastfed for 6 months. Furthermore, some researchers have suggested an alternative mechanism involving prolactin (PRL), the hormone responsible for milk production. PRL may inhibit proteins involved in hepatic lipogenesis [29, 30], such as CD36 glycoprotein and stearoyl-coenzyme A desaturase 1 (SCD1), thereby reducing the risk of steatotic liver disease. Specifically, PRL inhibits CD36, which is involved in fatty acid uptake, and SCD1, which plays a role in fatty acid synthesis, thus helping to regulate liver fat accumulation. Importantly, PRL levels remain consistently high throughout 24 h with frequent suckling episodes [31], as observed in EBF. This suggests that EBF may sustain the inhibitory effects on CD36 and SCD1 expression, further reinforcing its protective association with reduced NAFLD prevalence.

The present study demonstrated a higher prevalence of NAFLD than that reported in the CARDIA and KNHANES studies (33.8% vs. 6.4% vs. 15.2%, respectively). This difference could be attributed to various factors, including differences in underlying health conditions (GDM vs. uncomplicated pregnancy in both comparisons), ethnic groups (Asian vs. Asian vs. White or Black), and methods used to assess liver fat (transient elastography vs. computed tomography vs. hepatic steatosis index). Our study provides valuable insights into the epidemiology of NAFLD following GDM and highlights the potential role of breastfeeding for ≥6 months and EBF for 6 months in reducing NAFLD risk.

Table 3 Changes in participant characteristics between baseline and 1 year postpartum based on breastfeeding practice groups

	Breastfeeding practice group[a]												
	Group 1 ($n=57$)				Group 2 ($n=26$)				Group 3 ($n=47$)				
	Baseline	1 year	Change	*p*-value[b]	Baseline	1 year	Change	*p*-value[b]	Baseline	1 year	Change	*p*-value[b]	*p*-value[c]
Weight (kg)	67.8 ± 14.1	69.1 ± 16.2	1.3 ± 8.1	0.236	67.1 ± 9.9	69.0 ± 11.2	1.9 ± 4.1	0.024	59.1 ± 10.1	59.1 ± 9.6	0 ± 4.9	0.955	0.308
BMI (kg/m^2)	27.2 ± 5.2	27.7 ± 6.0	0.5 ± 2.6	0.178	27.2 ± 4.1	28.0 ± 4.5	0.8 ± 1.7	0.029	24.1 ± 3.4	24.1 ± 3.4	0 ± 2.1	0.978	0.298
WC (cm)	85.8 ± 10.2	90.5 ± 13.9	4.3 ± 9.7	0.004	89.5 ± 9.2	90.2 ± 8.7	0.7 ± 7.5	0.619	83.2 ± 10.5	87.8 ± 12.3	3.1 ± 7.3	0.116	0.162
FPG (mg/dL)	99.6 ± 32.8	110.3 ± 42.2	10.7 ± 35.6	0.027	90.3 ± 5.5	100.5 ± 11.5	10.2 ± 10.5	< 0.001	87.7 ± 10.7	96.6 ± 16.4	9.0 ± 10.9	< 0.001	0.673
Cholesterol (mg/dL)	214.3 ± 39.2	188.8 ± 33.8	−25.5 ± 33.6	< 0.001	223.7 ± 45.3	205.8 ± 41.0	−17.9 ± 27.3	0.003	227.5 ± 48.9	197.9 ± 36.1	−30.0 ± 35.6	< 0.001	0.171
TG (mg/dL)	154.9 ± 87.7	120.9 ± 62.0	−34.0 ± 72.7	< 0.001	141.9 ± 81.4	119.5 ± 51.0	−22.4 ± 76.2	0.147	93.0 ± 47.2	91.2 ± 59.3	−1.7 ± 60.8	0.845	0.740
LDL-C (mg/dL)	142.8 ± 37.4	127.9 ± 28.7	−14.9 ± 27.7	< 0.001	151.6 ± 39.0	143.2 ± 40.2	−8.4 ± 24.2	0.089	152.8 ± 48.4	132.4 ± 33.8	−20.4 ± 34.4	< 0.001	0.106
HDL-C (mg/dL)	57.0 ± 17.0	52.7 ± 13.3	−4.3 ± 13.7	0.020	57.5 ± 15.0	51.9 ± 14.2	−5.7 ± 8.9	0.003	69.5 ± 13.9	62.0 ± 12.4	−7.5 ± 11.3	< 0.001	0.345
Prediabetes	14 (24.6)	31 (54.4)	17 (29.8)	< 0.001	1 (3.8)	14 (53.8)	13 (50.0)[d]	< 0.001	6 (12.8)	16 (34.0)	10 (21.2)	0.002	0.049
Metabolic syndrome	18 (31.6)	28 (49.1)	10 (17.5)[d]	0.041	6 (23.1)	13 (50.0)	7 (26.9)[d]	0.065	4 (8.5)	5 (10.6)	1 (2.1)	1.000	0.019

Data are presented as the mean ± SD or n (%)

Abbreviations: BMI body mass index, *EBF* exclusive breastfeeding, *FPG* fasting plasma glucose, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *SD* standard deviation, *TG* triglycerides, *WC* waist circumference

[a] Group 1 = breastfeeding for < 6 months; group 2 = breastfeeding for ≥ 6 months and EBF for < 6 months; and group 3 = breastfeeding for ≥ 6 months and EBF for 6 months

[b] Changes over time within each group were analyzed using the paired t-test or McNemar's test

[c] Changes between groups were analyzed using a one-way analysis of covariance, with the baseline value of each parameter as a covariate, or using the chi-squared test

[d] $p < 0.05$, compared with group 3

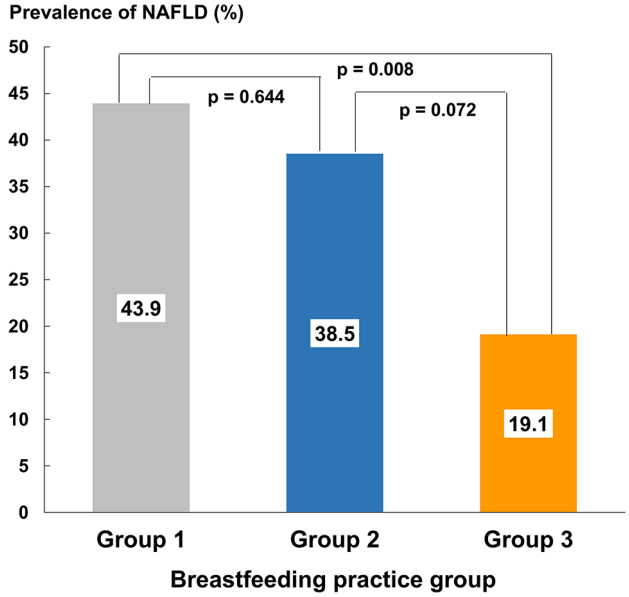

Fig. 2 Prevalence of non-alcoholic fatty liver disease among different breastfeeding practice groups. Group 1 = breastfeeding for < 6 months; group 2 = breastfeeding for ≥ 6 months and EBF for < 6 months; and group 3 = breastfeeding for ≥ 6 months and EBF for 6 months. *Abbreviations: EBF* exclusive breastfeeding. *NAFLD* non-alcoholic fatty liver disease

Additionally, the association between the use of progestin-only contraceptives and NAFLD, which mirrors animal study data showing that progesterone can increase hepatic lipid content and plasma lipid levels [32], underscores the importance of informed contraceptive choices postpartum. In light of these findings, healthcare professionals should consider advising postpartum women not only on the importance of postpartum glucose testing but also on the benefits of prolonged and intensive breastfeeding and the careful selection of contraceptive methods to mitigate the risk of developing NAFLD [33].

However, while our study suggests a protective association between breastfeeding and reduced NAFLD, the duration of this effect after weaning is not well understood. To address this gap, we recommend further longitudinal studies that include serial liver fat quantifications over an extended period after weaning. Such research could provide clinicians with a deeper understanding of how breastfeeding impacts the development and progression of NAFLD and elucidate the underlying pathophysiological mechanisms at play.

The strengths of our study include the use of multiple methods to accurately assess breastfeeding practices, thereby enhancing the quality and reliability of breastfeeding data. These methods encompassed interviews conducted during follow-up visits, meticulous data recording by participants using a provided calendar, and prospective assessment of breastfeeding status documented in the hospital's electronic database during follow-up visits of the babies. Additionally, liver fat evaluation was conducted with strict criteria to ensure the precision of all CAP measurements. Importantly, our study contributes new evidence demonstrating that the combination of prolonged and intensive breastfeeding is associated with a lower amount of liver fat in the postpartum period among women with recent GDM. These findings underscore the potential benefits of sustained and dedicated breastfeeding in reducing liver fat accumulation and enhancing postpartum liver health in this at-risk population.

This study has some limitations. First, liver fat levels were not compared among groups before breastfeeding, which could have provided a baseline measure for more accurate comparison. Second, different baseline characteristics across groups may have influenced the study outcomes. However, we attempted to mitigate this bias by using case pairs from baseline to 1 year postpartum. Third, we did not collect data on participants' dietary intake, which could have impacted the study's results.

Additionally, the CAP cutoff of ≥302 dB/m, while specific for detecting NAFLD [24], may have excluded milder cases. Moreover, despite the total number of participants exceeding the required sample size, the number of women in group 2 was relatively low. The limited number of NAFLD cases also constrained the number of factors we could control for in the regression model, as per the rule of thumb requiring at least 10 outcome events per predictor variable [34]. Lastly, the study's focus on a homogeneous cohort of Asian patients limited the generalizability of the findings. Future research should validate these results in more diverse populations.

Table 4 Unadjusted and adjusted odds ratios of non-alcoholic fatty liver disease 1 year postpartum for participants in groups 2 and 3

	Breastfeeding practice group[a]				
	Group 1 (*n* = 57)	Group 2 (*n* = 26)		Group 3 (*n* = 47)	
		Unadjusted OR (95% CI)	Adjusted OR[b] (95% CI)	Unadjusted OR (95% CI)	Adjusted OR[b] (95% CI)
NAFLD	1.00 (reference)	0.80 (0.31, 2.06)	0.80 (0.27, 2.41)	0.30 (0.12, 0.74)	0.34 (0.14, 0.95)

Abbreviations: BMI body mass index, *CI* confidence interval, *EBF* exclusive breastfeeding, *FPG* fasting plasma glucose, *NAFLD* non-alcoholic fatty liver disease, *OR* odds ratio

[a] Group 1 = breastfeeding for < 6 months; group 2 = breastfeeding for ≥ 6 months and EBF for < 6 months; and group 3 = breastfeeding for ≥ 6 months and EBF for 6 months

[b] Adjusted for age, severity of GDM, method of contraception used, baseline BMI, and FPG

Conclusions

Longer duration and higher intensity of breastfeeding were associated with lower liver fat levels and reduced NAFLD prevalence at approximately 1 year postpartum in women with previous GDM. Our findings suggested that breastfeeding for ≥6 months and EBF for 6 months might be a promising intervention strategy to reduce NAFLD risk after GDM.

Abbreviations

BMI	Body mass index
CI	Confidence interval
EBF	Exclusive breastfeeding
FLD-GDM	Fatty Liver Disease after Gestational Diabetes Mellitus
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
HDL-C	High- density lipoprotein cholesterol
HIV	Human immunodeficiency virus
LSM	Liver stiffness measurement
MetS	Metabolic syndrome
NAFLD	Non-alcoholic fatty liver disease
OR	Odds ratio
PRL	Prolactin
SCD1	Stearoyl-coenzyme A desaturase 1
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TG	Triglycerides
UNICEF	United Nations Children's Fund
WC	Waist circumference
WHO	World Health Organization

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Author contributions

SS: Conceptualization, Methodology, Validation, Investigation, and Writing - Reviewing and Editing. CP: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data Curation, Writing – Original Draft, Writing – Reviewing and Editing, and Funding acquisition.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Vajira Institution Review Board (approval no. 117/2564). The study was performed in accordance with the Declaration of Helsinki. All participants agreed to participate in the study and provided written informed consent.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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