Early Postpartum Lipid Profile in Women with and Without Gestational Diabetes Mellitus: Results of a Prospective Cohort Study

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Abstract

Background: Dyslipidemia is a well-known risk factor of cardiovascular disease. Few studies focused on early postpartum lipids profile, particularly in women with gestational diabetes mellitus.

Objectives: This study aims at determining the levels of total cholesterol, triglycerides LDL-C, HDL-C, and VLDL-C at 6 to 12 weeks postpartum in women with gestational diabetes, comparing them to lipids profiles of controls and identifying independent risk factors of dyslipidemia in 2 studied groups.

Methods: Life after gestational diabetes, Ahvaz study (LAGAs), was started on March 2015. This was an ongoing population-based cohort study that aimed at investigating metabolic outcomes of gestational diabetes mellitus and comparing them with healthy groups. Up to February 2016, during the first 11 months sampling, 176 women with gestational diabetes and 86 healthy mothers underwent FBS, 75-g 2- hour oral glucose tolerance and fasting lipids tests (including total cholesterol, triglyceride, LDL- cholesterol, HDL -cholesterol, and VLDL-cholesterol) in 6 to 12 weeks after delivery.

Results: Overall prevalence of dyslipidemia was 73.7%. Most common forms of dyslipidemia in 2 groups were HDL-C < 50 and raised total cholesterol (T-C $\geq$ 200). Women with gestational diabetes had higher total cholesterol, triglyceride, LDL-C, and VLDL-C compared with controls. Prevalence of total cholesterol $\geq$ 200, triglyceride $\geq$ 150, HDL-C < 50 (md/dL), and LDL-C $\geq$ 130 (md/dL) was 37.5%, 22.2%, 43.8%, and 27.8 in GDM women 6 to 12 weeks after delivery, respectively; 73.3% (129/176 (of GDM women had at least one abnormal values of lipids. Pre-pregnancy BMI $\geq$ 25 and history of GDM in first relatives were associated risk factors for dyslipidemia in women with gestational diabetes. In multivariate analysis, only BMI $\geq$ 25 in healthy group remained as an independent risk factor for dyslipidemia 6 to 12 weeks postpartum.

Conclusions: Dyslipidemia is highly prevalent in women with and without GDM at 6 to 12 weeks postpartum, particularly in overweight and obese women. Dyslipidemia and obesity are both modifiable risk factors for cardiovascular disease.

Keywords: Postpartum, Dyslipidemia, Gestational Diabetes Mellitus, Obesity, Cohort Study

1. Background

Dyslipidemia is a well-known independent risk factor for cardiovascular disease (CVD) and progression of atherosclerosis. Based on a 30-year cohort study, each increase of 10 mg/dL in total cholesterol is associated with 5% increase in total mortality and 9% in mortality from cardiovascular disease (1).

Normal pregnancy is associated with many changes in maternal lipid profile. These alterations include rising total cholesterol, HDL-C, LDL-C, and specifically elevated triglycerides (2). Pregnancy alteration of lipid metabolism may permanently remain after delivery. Maternal hyper-triglyceridemia is associated with increased risk of cardiovascular disease in later years of life (3).

Gestational diabetes mellitus (GDM) is a rising metabolic disorder, which complicates 1% to 28% of pregnancies (4). Similar to dyslipidemia, history of GDM is considered a potential risk factor for cardiovascular diseases, among middle-aged women (5). Moreover, women with GDM have an increased risk for Type 2 diabetes mellitus, cardiovascular disease, and metabolic syndrome years after pregnancy. Abnormal lipid profile, more than it was reported in normal pregnancy, has been reported in pregnancies exposed to gestational diabetes (6).

However, these findings are generally inconsistent (7-

9). In addition, it may be possible that the results of these studies only represent long-term investigation. Moreover, it is not clear whether GDM is an independent predicator of future metabolic outcomes (including hyperlipidemia) or its relationship has been due to pre-pregnancy obesity and/or future Type 2 diabetes, metabolic syndrome, or cardiovascular morbidity (5, 10).

Usually women with GDM are not screened for dyslipidemia because absolute risk of dyslipidemia and cardiovascular disease is low in this age group (11). This issue is one of the main causes of unclear association between GDM and dyslipidemia.

Furthermore, short- and long-term metabolic outcomes of GDM are unclear after applying the IADPSG as a new criterion (12). Despite these findings, postpartum screening for lipid abnormalities and other cardiovascular risk factors has been neglected in women with gestational diabetes (13). In addition, few studies focused on early postpartum lipids profile, particularly in women with GDM.

Our study aimed at determining the rate of early dyslipidemia at 6 to 12 weeks postpartum. Moreover, the contributing risk factors and potential differences with peers in the control group were assessed according to IADPSG criteria.

2. Objectives

In this study, we aimed at determining the levels of total cholesterol, triglycerides LDL-C, HDL-C, and VLDL-C at 6 to 12 weeks postpartum in women with gestational diabetes compared with these components in women with normal glucose status during recent pregnancy and identifying potential risk factors of dyslipidemia in the 2 studied groups.

3. Methods

3.1. Study Design and Setting

Life after gestational diabetes, Ahvaz study (LAGAs), is an ongoing population-based cohort study that investigates potential metabolic outcomes of gestational diabetes mellitus in mothers and their offspring, compares them with those of the healthy population during pregnancy, 6 to 12 weeks postpartum, and follows the participants for 2 years after delivery. We established the first gestational diabetes clinic in Khuzestan province specifically for this project in Golestan teaching hospital in Ahvaz in October 2013. Ahvaz the capital of Khuzestan (Southwest of Iran), where the study is currently in progress, has a high birth rate, high prevalence of obesity, metabolic syndrome,

and dyslipidemia in the general population (14-16). Moreover, a high incidence of GDM was recently reported in this area using IADPSG criteria (29.9%) (17).

3.2. Study Population and Biochemical Assessment During Pregnancy

The study started from March 2015. Pregnant women attending to 25 urban public and private centers seeking prenatal care were recruited and underwent initial assessment using fasting plasma glucose (FPG) in the first trimester. These centers applied single approach for screening, treatment, and management of GDM. Screening oral glucose tolerance test (OGTT) was performed at 24 to 28 weeks of gestation for those women with normal results.

A list of women with GDM and their peers in the control group, with details of contact information, was sent to the research team by 25 prenatal care centers, and eligible women were referred to Golestan hospital (the cohort center) if they agreed to participate in the study. Various methods of communication including direct contact by phone, SMS texts via phone line, or social networks were used to encourage women to participate and return for postpartum follow-up.

3.2.1. Inclusion Criteria

-Women with GDM in first trimester diagnosed by FPG
-Women with GDM in second or third trimester diagnosed by 75-g OGTT
-Availability of clinical and medical records or health profile for pre-pregnancy details

3.2.2. Exclusion Criteria

-Pre-gestational diabetes Type 1 or Type 2 (10 cases)
-Women with FPG $\geq$ 126 mg/dL at initial assessment in first trimester (22 cases)
-Planning to move from Ahvaz within the subsequent 2 years
-Women who refused to continue at any stage of the study

Sample size was calculated considering metabolic outcomes by comparing the 2 proportions formulas with a power of 80% and 95% confidence interval (Equation 1).

$$n = \left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 \left[P_1\left(1 - P_1\right) + P_2\left(1 - P_2\right)\right]/\left(P_1 - P_2\right)^2 \tag{1}$$

Primary outcome was postpartum glucose intolerance, with $\alpha = 0.05$, $\beta = 0.2$, $P_1 = 0.1$ (cumulative incidence of diabetes 2 years after delivery in women with gestational diabetes) (18), $P_2 = 0.01$ (expected incidence of diabetes in Iranian healthy women in the same age group) (19), and

primary sample size was calculated (143 women in each group). We predicted 30% patient attrition during 2 years follow-up, therefore, 410 women (205 participants in each group) was need.

Sequential sampling was conducted. All eligible women with gestational diabetes diagnosed by IADPSG criteria in 25 centers were selected as exposed group and invited to participate in the study. From March 2015 to February 2016, of 800 women who were diagnosed as GDM, 176 women (22%) returned at 6 to 12 weeks postpartum (Flowchart 1). Recruitment will be continued until reaching the required sample size. We randomly selected pregnant women in control group in the same sittings in the same age group.

We used interviewer-administered questionnaires to collect the data related to socio-demographic characteristics, medical and obstetric history, potential risk factors of GDM and dyslipidemia, and details of gestational diabetes management during pregnancy. Interviewers held by bachelors of public health and recorded pregnancy-related data at the prenatal care centers and measured anthropometrics characteristics under supervision of trained researchers.

Pre-pregnancy body weight was recorded using medical and health profile. Anthropometric measurements including weight, height, waist circumference, blood pressure, and hip circumference were measured at baseline visit during pregnancy. Weight and blood pressure measurements were repeated at each pregnancy visit.

3.3. Definition of Gestational Diabetes Mellitus and Dyslipidemia

We used international association of diabetes and pregnancy study groups (IADPSG) criteria for diagnosis of gestational diabetes; only one abnormal value was considered as GDM either $\geq$ 92 mg/dL for fasting glucose or $\geq$ 180 mg/dL for 1-hour plasma glucose after drinking 75-gr glucose or $\geq$ 153 mg/dL for 2-hour plasma glucose level.

Dyslipidemia was defined as having at least one lipid abnormality inclusive of total cholesterol $\geq$ 200 mg/dL, triglyceride $\geq$ 150 mg/dL, LDL-cholesterol $\geq$ 130 mg/dL, or HDL-cholesterol < 50 mg/dL in accordance with adult treatment panel (ATP III) criteria.

3.4. Postpartum Data Collection

Short forms related to feto-maternal outcomes and details of delivery were filled out during 3 to 5 days postpartum at 2 main centers to screen neonatal hypothyroidism. Other postpartum questionnaires were completed by a member of the research team at our cohort center 6 to 12 weeks postpartum (between fasting sampling and 2 hours after drinking 75 -gr glucose). Physical activity and food habits of participants and potential postpartum problems among mothers or their infants were recorded. A second comprehensive questionnaire will be completed within 2 years postpartum based on our study protocol (6 months, 1 year, and 2 years postpartum).

3.5. Postpartum Biochemical and Clinical Assessment

From March to February 2016, during the first 11 months of the study, 176 women with gestational diabetes and 86 healthy mothers underwent FPG, 75-g 2-hour oral glucose tolerance, and fasting lipids tests (including total cholesterol, triglycerides, LDL- cholesterol, HDL- cholesterol, and VLDL-cholesterol) at 6 to 12 weeks after delivery. These tests will be repeated annually for up to 2 years postpartum. Blood samples were taken after at least 10 hours overnight fasting by 2 expert nurses and transported to laboratory of diabetes research center, where blood tests were performed by 2 expert technicians who were not aware of the study objectives.

Blood serum was used to measure the following tests: FBS, total Cholesterol, triglyceride, and HDL-C (by Pars Azmoon Inc., Iran by BT3000 autoanalizer). LDL was calculated by the Friedewald formula (LDL-cholesterol = total cholesterol-HDL-cholesterol-triglyceride/5 mg/dl) if triglyceride level was 400 mg/dL or lower. LDL- cholesterol was only measured chemically when triglyceride level was more than 400 mg/dL [20].

Blood pressure was taken by mechanical sphygmomanometer after at least 5 minutes rest, and measurements were repeated 30 minutes later. Having a systolic blood pressure $\geq$ 140 mm Hg or diastolic blood pressure $\geq$ 90 mm Hg, or use of antihypertensive drug was defined as hypertension. Weight, waist circumference, blood pressure, and hip circumference were measured at 6 to 12 weeks postpartum and will be repeated during the 2 years follow-up. Body mass index (BMI) was calculated, and BMI lower than 25 (kg/m^2), 25 - 29.9 (kg/m^2) and $\geq$ 30 (kg/m^2) was considered as normal, overweight, and obesity, respectively.

Waist circumference was measured at the midpoint between the lowest rib and the upper lateral border of the right iliac crest and hip circumference at the point of maximum hip diameter using a standard measuring tape.

3.5.1. Quality Control

Quality control procedure included the following steps: pilot study, standardizing the questionnaires and check lists using Delphi method, exact selection of exposed and control groups, training the questioners and bachelors for physical exam, anthropometric measurements and blood sampling based on standard methods, attendance of at least one of the research team members in all

process of postpartum follow-up in the cohort center, repeat 10% to 15% of normal biochemical tests and duplicate all abnormal values, continue monitoring next visit of mothers and sending a reminder if mothers did not return in the specified date. All the scales for anthropometric measurements were calibrated every day. The interview was repeated for 10% of participants during 40 days after the first visit (Kappa statistics = 0.74).

Laboratory tests were performed using standardized automatic devices in the laboratory of Ahvaz Jundishapur diabetes research center. Technical error of measurement (TEM) was estimated for the observer teams with an anthropometry expert and found to have acceptable bias.

3.6. Statistical Analysis

All analyses were conducted using statistical package for the social sciences (SPSS Version 22). Independent sample t- tests, χ^2 and Fisher's exact test analysis were performed. Univariate and backward multivariate logistic regression were used to assess predictors of early postpartum lipids abnormality. Variables with significant level of 0.2 or less were tested in multivariate analysis. P values of < 0.05 were considered statistically significant.

3.7. Ethical Consideration

Ahvaz Jundishapur University of Medical Sciences ethical committee approved the study protocol (ethic code: IR.AJUMS.REC.1394.252). Written informed consent as obtained from each participant. Participation of women in the present study was voluntary and aims of the study were described to all the participants. All procedures were conducted with careful security considerations. Clinical evaluation and blood tests were free of charge and a copy of their laboratory reports was submitted to the patients for future reference.

4. Results

4.1. Descriptive Characteristics

In this study, 262 women aged 17 to 45 years underwent a postpartum OGTT and completed lipid tests (176 women with gestational diabetes and 86 cases with normal glycaemia in pregnancy) at 6 to 12 weeks after delivery. Demographic, clinical, and biochemical characteristics of women with or without gestational diabetes are presented in Table 1. Most participants (92.4%) were homemakers. Prevalence of overweight and obesity was 40.5% (41.5% in women with GDM and 38.4% in controls) and 26.7% (30.1% in women with GDM and 19.8% in controls), respectively. The overall prevalence of dyslipidemia was 73.7% (55.8% in women with normal pre pregnancy BMI and 82.4% in

women who were overweight or obese). TC/ HDL-C $\geq$ 4 was observed in 29% of women. Most common forms of dyslipidemia in the 2 groups were raised total cholesterol (T-C $\geq$ 200) and HDL-C < 50. Women with gestational diabetes had higher total cholesterol, triglyceride, LDL-C, and VLDL-C compared to controls (P < 0.05) (Table 1).

4.2. Lipid Profile in Women with GDM

Of women with GDM, 25.5% had total cholesterol of 200 to 239 mg/dL (14% in women who had normal pregestational BMI, and 31.2% in overweight or obese women), and 12.5% had total cholesterol of 240 or more (8% in women with normal BMI range, 14.3% in women with BMI $\geq$ 25). LDL-C equal or more than 160 mg/dL was observed in 8% of women with GDM (only one case in women with normal BMI); 38.1% of women had 2 or more abnormal components in their lipid profile. More details of postpartum dyslipidemia in women with and without gestational diabetes are presented in Table 2.

4.3. Lipid Profile in Women Without GDM

In 24.4% (21/86) of non- GDM women, total cholesterol was 200 to 239 mg/dL (22.2% in women with normal prepregnancy BMI and 26% in women who had BMI $\geq$ 25). None of the women who were in healthy group had total cholesterol of 240 mg/dL or more; 26.8% of controls had 2 or more abnormal values in their lipid profile (7% more than 2 abnormal components). LDL-C $\geq$ 160 was observed in 2 women in the control group.

4.4. Univariate and Multivariate Analysis

Prevalence of dyslipidemia based on potential risk factors is presented in Table 3. Details of postpartum dyslipidemia in women with normal BMI or BM $\geq$ 25 kg/m², with and without gestational diabetes are presented in Table 4.

Pre- pregnancy BMI $\geq$ 25 and history of GDM in first relatives (mother or sister) were associated risk factors for dyslipidemia in women with gestational diabetes after adjustment of significant risk factors in univariate regression analysis (Table 5). In multivariate analysis, only BMI $\geq$ 25 in healthy group remained as an independent risk factor for dyslipidemia 6 to 12 weeks Postpartum (Table 5).

5. Discussion

Lipid metabolism changes during pregnancy and following pregnancy abnormal lipid profile may remain for years. Based on our results, prevalence of dyslipidemia was high at 6 to 12 weeks postpartum (73.7%). Raised cholesterols (total cholesterol, LDL-cholesterol), high level of triglyceride, and low HDL-cholesterol were prevalent
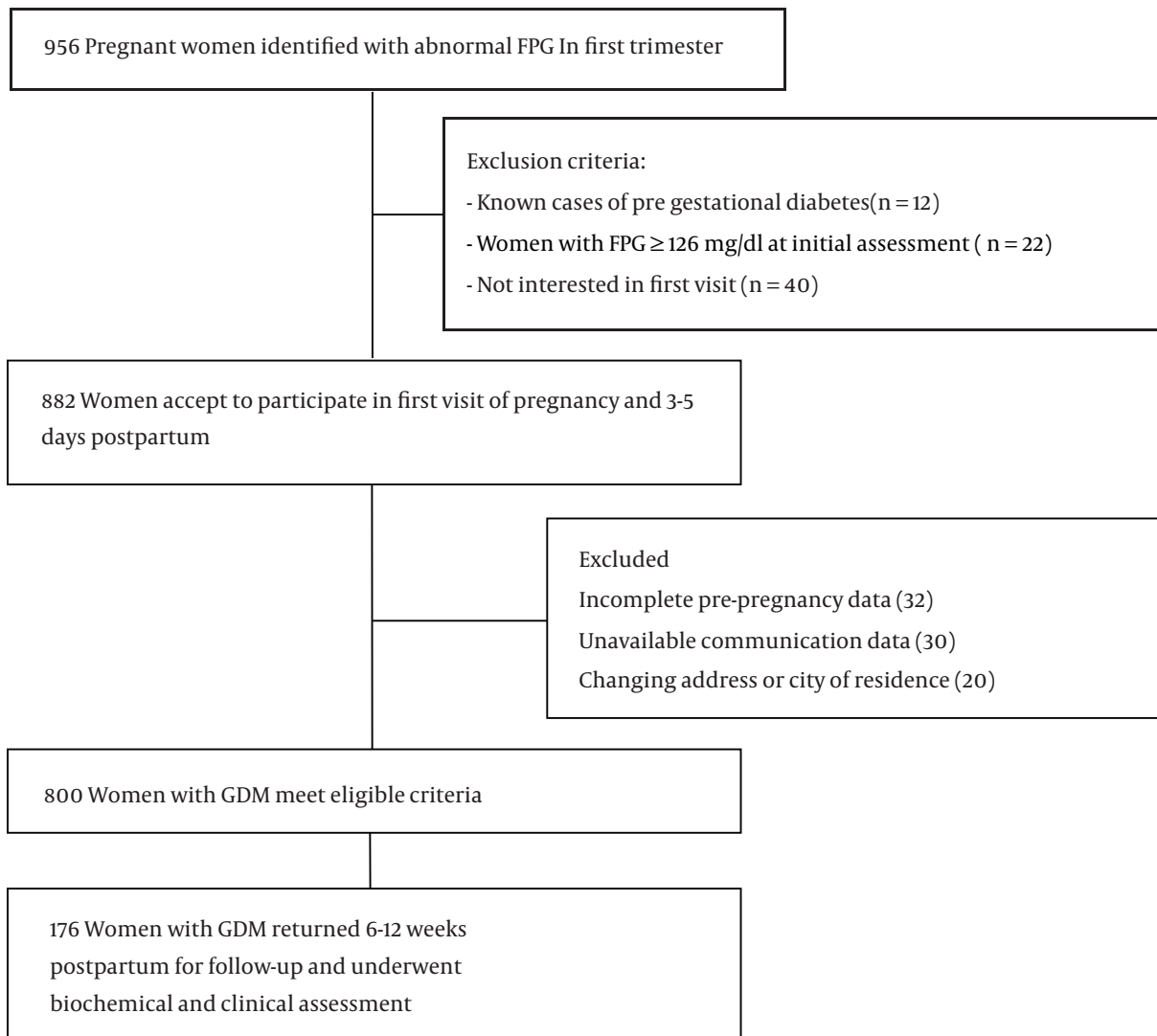
Figure 1. Flowchart of the Participants in the Cohort Study

in both women with and without gestational diabetes. Women with gestational diabetes had significantly higher total cholesterol, glyceride, LDL-C and VLDL-C compared to controls. Rate of postpartum elevated total cholesterol ($\geq$ 200 mg/dL) was higher in women with GDM (37.5% versus 22.4% in controls) (P = 0.03) (Table 2). Overweight and obesity (BMI $\geq$ 25) were common risk factors associated with postpartum dyslipidemia in both women exposed to GDM and their peers in the control group (Table 5). Raised total cholesterol ($\geq$ 200 mg/dL) and low HDL - C (< 50 mg/dL) were 2 most common forms of dyslipidemia in both groups (GDM and controls) (Table 2). In women with GDM, positive history of gestational diabetes among

first-degree relatives (mother or sisters) was found to be another significant risk factor associated with lipid abnormalities (Table 5).

5.1. Postpartum Lipids Changes in Short and Long-Term Follow-up

Consistent with our results, high rate of lipid abnormalities and long-term alteration of lipid profile after pregnancy were reported by Potter and Nestel (21). They found that elevated total cholesterol in pregnancy returned to near pre- pregnancy level at 52 weeks postpartum. Darmody and Postle also observed normal values for total cholesterol at 40 weeks postpartum (22). Van

Table 1. Demographic, Clinical and Biochemical Characteristics of Women with or Without Gestational Diabetes

Characteristics	Total (N = 262), Mean ± SD	GDM Group (N = 176), Mean ± SD	Control Group (N = 86), Mean ± SD	P Value[a]
Age (years)	29.52 ± 5.32	29.68 ± 5.25	29.19 ± 5.49	0.49
Weight before pregnancy	70.17 ± 12.19	71.51 ± 12.10	67.44 ± 11.97	0.01
Weight in last month of pregnancy	81.27 ± 12.92	82.33 ± 12.92	79.10 ± 12.72	0.05
Pre-pregnancy BMI (kg/m²)	27.21 ± 4.49	27.82 ± 4.41	25.98 ± 4.41	0.002
Systolic BP pregnancy	112.88 ± 17.93	114.11 ± 20.26	111.39 ± 11.79	0.21
Diastolic BP pregnancy	68.53 ± 11.93	69.28 ± 12.38	66.97 ± 10.85	0.14
Triglyceride(mg/dL)	108.24 ± 24.91	115.64 ± 73.74	93.09 ± 53.84	0.01
Total cholesterol (mg/dL)	185.91 ± 43.76	191.81 ± 47.48	172.84 ± 31.90	0.002
HDL-C (mg/dL)	51.24 ± 10.13	51.77 ± 9.76	50.13 ± 10.83	0.22
LDL-C (mg/dL)	111.20 ± 30.28	114.62 ± 30.94	104.18 ± 28.10	0.009
VLDL (mg/dl)	21.20 ± 11.76	22.53 ± 12.03	18.51 ± 10.74	0.009
TC/ HDL-C	3.69 ± 0.83	3.76 ± 0.85	3.56 ± 0.76	0.07
Mother education, N (%)				0.27
< High school	83 (31.7)	54 (30.7)	29 (33.7)	
High school	112 (42.7)	81 (46.0)	31 (36.0)	
Collage	67 (25.6)	41 (23.3)	26 (30.2)	
Ethnicity, N (%)				0.16
Fars	85 932.4)	63 (35.8)	22 (25.6)	
Lor	56 (21.4)	33(18.8)	23 (26.7)	
Arab	121 (46.2)	80 (45.5)	41 (47.7)	
Gravidity, N (%)				0.89
1	71 (27.1)	49 (27.8)	22 (25.6)	
2	89 (34.0)	57 (32.4)	32 (37.2)	
3	58 (22.1)	40 (22.7)	18 (20.9)	
≥ 4	44 (16.8)	30 (17.0)	14 (16.3)	
Cesarean delivery, N (%)	152 (58)	100 (56.8)	52 (60.5)	0.57
Pre-gestational overweight or obesity, N (%)	176 (67.2)	126 (71.6)	50 (58.1)	0.02
History of family DM, N (%)	132 (50.4)	98 (55.7)	34 (32.5)	0.01
History GDM in first relatives[b], N (%)	85 (41.3)	64 (46.7)[c]	21 (30.4)[c]	0.02
Breast feeding, N (%)	199 (76.0)	131 (74.4)	68 (79.1)	0.40

Abbreviations: BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; TC/ HDL-C, total cholesterol high density lipoprotein cholesterol; DM, diabetes mellitus; GDM, gestational diabetes mellitus.
[a]Using t-test or chi square test.
[b]GDM in mother or sister.
[c]56 missing cases (unknown history of GDM in family, 39 cases in GDM group, and 15 cases in controls).

Stiphout et al. showed higher total cholesterol and lower HDL-C in women who had at least one pregnancy compared with nuligravida women (23). Similar to our findings, Jimes et al. reported persistent abnormal cholesterol 40 days postpartum. Recently, Prairie et al. showed high to-tal cholesterol and LDL-C levels in women with depression at 1 to 14 weeks postpartum (24). In another report, HDL-C decreased to pre- pregnancy level during 10 years after the first pregnancy (25).

Table 2. Comparison of Dyslipidemia and its Components in Women with and Without Gestational Diabetes

Variable	Total (N = 262), N (%)	GDM Group (N = 176), N (%)	Control Group (N = 86), N (%)	P Value
TC ≥ 200 (mg/dL)	87 (33.2)	66 (37.5)	21 (24.4)	0.03
Triglisiride ≥ 150 (mg/dL)	51 (19.5)	39 (22.2)	12 (14.0)	0.11
HDL-C < 50 (mg/dL)	125 (47.7)	77 (43.8)	44 (55.8)	0.06
LDL-C ≥ 130 (mg/dL)	66 (25.2)	49 (27.8)	17 (19.8)	0.15
TC/HDL ≥ 4	79 (29.0)	53 (30.1)	23 (26.7)	0.57
Dyslipidemia***	193 (73.7)	129 (73.3)	64 (74.4)	0.84

Table 3. Distribution of Potential Risk Factors of Dyslipidemia in Women With and Without Gestational Diabetes

Variable	Dyslipidemia[a] GDM Group, N (%)	P Value[b]	Dyslipidemia[a] Non-GDM Group, N (%)	P Value[b]
Mother ethnicity		0.18		0.74
Fars	43 (68.3)		6 (72.7)	
Lor	22 (66.7)		16 (69.6)	
Arab	64 (80.0)		32 (78.0)	
Gravidity		0.04		0.35
1 - 2	72 (67.9)		42 (77.8)	
> 2	57(81.4)		22 (68.8)	
Mother education		0.04		0.06
< High school	41 (75.9)		22 (75.9)	
High school	64 (79)		19 (61.3)	
Collage	24 (58.5)		23 (88.5)	
Kind delivery		0.91		0.03
Vaginal	56 (73.7)		21 (61.8)	
Cesarean	73 (73.0)		43 (82.7)	
Pre-pregnancy BMI		0.001		0.001
Normal	28 (56.0)		20 (55.6)	
Overweight or obesity	101 (80.2)		44 (88.0)	
History GDM in first relatives		0.01		0.93
Yes	54 (84.4)		37 (77.1)	
No	48 (65.8)		16 (76.2)	
Previous GDM[c]		0.70		0.32
Yes	20 (76.9)		6 (100.0)	
No	74 (73.3)		43 (75.4)	
Breast feeding	93 (71%)	0.23	52 (76.5)	0.39
Formula or combined	36 (80.0)		12 (66.7)	

[a]At least one abnormal lipids inclusive of cholesterol ≥ 200 mg/dL, triglyceride ≥ 150 mg/dL, LDL-cholesterol ≥ 130 mg/dL, or HDL-cholesterol < 50 mg/dL.
[b]P value calculated by Chi square test.
[c]In multiparous women.

Table 4. Details of Postpartum Dyslipidemia in Women With Normal BMI or BM $\geq$ 25 kg/m^2, With and Without Gestational Diabetes

Variable	GDM Group (N = 176)		P Value	Non-GDM Group(N = 86)		P Value
	Normal Weight	Overweight or Obese		Normal Weight	Overweight or Obese	
TC $\geq$ 200 (mg/dL)	11 (22.0)	55 (43.7)	0.007	8 (22.2)	13 (26.0)	0.68
Triglisiride $\geq$ 150 (mg/dL)	6 (12.0)	33 (26.2)	0.04	2 (5.6)	10 (20.0)	0.06[a]
HDL-C < 50 (mg/dL)	17 (34.0)	60 (47.6)	0.10	13 (36.1)	35 (70)	0.002
LDL-C $\geq$ 130 (mg/dL)	8 (16.0)	41 (32.5)	0.02	6 (16.7)	11 (22.0)	0.54
TC/HDL $\geq$ 4	5 (10.0)	48 (38.1)	< 0.001	4 (11.1)	19 (38.0)	0.001
Dyslipidemia[b]	28 (56.0)	101 (80.2)	0.001	20 (55.6)	44 (88.0)	0.001

[a]Fisher's exact test.
[b]At least one abnormal lipids inclusive of cholesterol $\geq$ 200 mg/dL, triglyceride $\geq$ 150 mg/dL, LDL-cholesterol $\geq$ 130 mg/dL, or HDL-cholesterol < 50 mg/dL.

Table 5. Independent Risk Factors for Early Postpartum Dyslipidemia (At Least One of Abnormal Components) in Women with and Without Gestational Diabetes Using Univariate and Multivariate Logistic Regression Analysis

Variables	B[a]	SE[a]	Unadjusted ORs	95% CI	P Value	B[b]	SE[b]	Adjusted ORs[c]	95% CI	P Value
				GDM Group						
Mother ethnicity	0.30	0.19	1.36	0.93 - 1.97	0.10	0.27	0.24	1.31	0.81 - 2.10	0.26
Gravidity > 2	0.28	0.16	1.33	0.95 - 1.86	0.087	0.20	0.23	1.22	0.77 - 1.95	0.38
Mother education	0.40	0.23	0.66	0.41 - 1.05	0.080	0.08	0.32	0.91	0.48 - 1.72	0.78
History of family DM	0.60	0.34	1.83	0.93 - 3.59	0.078	9.37	0.50	0.96	0.36 - 2.57	0.94
Pre-pregnancy Overweight or obesity	0.65	0.23	1.93	1.21 - 3.06	0.005	0.88	0.28	2.42	1.38 - 4.24	0.002
BP systolic pregnancy	0.01	0.01	1.01	0.99 - 1.03	0.18	0.01	0.01	1.01	0.99 - 1.04	0.20
History GDM in first relatives[d]	1.03	0.42	2.81	1.22 - 6.45	0.015	1.06	0.44	2.91	1.23 - 6.88	0.015
				Non GDM Group						
Cesarean delivery	1.08	0.50	2.95	1.09 - 8.01	0.033	0.77	0.56	2.17	0.72 - 6.51	0.167
Systolic blood pressure pregnancy	0.06	0.02	1.06	1.008 - 1.12	0.025	0.05	0.03	1.05	0.99 - 1.12	0.068
Pre-gestational overweight or obesity	1.02	0.40	2.78	1.26 - 6.12	0.011	0.88	040	2.37	1.07 - 5.23	0.032

[a]Using univariate regression.
[b]Using multivariate regression.
[c]The model is adjusted for covariates with statistical P value less than 0.2 in the univariate regression analysis.
[d]History of GDM in mother or sister.

5.2. Comparison of Postpartum Lipids Levels in Women with GDM and Controls

We observed significant differences in levels of lipid components between women with gestational diabetes and controls (Table 1). Consistent with our results, total cholesterol level and triglycerides in women with history of GDM were elevated in postpartum compared with controls (7, 26, 27). Increased low-density lipoprotein (LDL) was reported in Caucasian women 6 years after GDM pregnancy (28, 29), Retnakaran et al. reported significant differences in total cholesterol, LDL, triglycerides, total cholesterol to HDL ratio with glucose status in pregnancy at 3 months postpartum in Canadian women (30). However, Montelongo et al. found no significant difference between exposed GDM women and controls during 3 years postpartum (31). Higgins et al., similar to our results, reported significant higher levels of total cholesterol, higher LDL-

C, and triglycerides in women with GDM compared to healthy women 6 weeks postpartum (32).

5.3. Comparison of Postpartum Dyslipidemia Rate and Its Components in GDM and Controls

In our study, prevalence of dyslipidemia was 73.3% in women with GDM in early postpartum weeks. High rate of dyslipidemia in women with GDM in early postpartum weeks has been reported in few previous studies. However, our estimation was higher than what was reported in Ireland (52%) (32) and Canada (50%) (33).Use of different criteria for definition of dyslipidemia (TC/HDL $\geq$ 4 in Edwards et al. report on Canadian women and Australian recommended standards in Australian study) may be one of the reasons for observing such differences between our results and that of the literature. High rate of dyslipidemia in our report is consistent with previously reported rate among urban middle-aged Iranians women (66.5%) (34); and this rate was 85.1% among women older than 20 years in Ahvaz using ATP III criteria (14).

Based on our finding, raised total cholesterol, raised LDL-C, and raised triglyceride were identified in 37.5%, 27.8 % and 22.2% of women with gestational diabetes, respectively. Higgins et al. in Ireland reported the following abnormal values: (T-C $\geq$ 200, LDL-C $\geq$ 130, triglisird $\geq$ 150) 44%, 33%, and 16%, respectively (32). Excess total cholesterol, LDL-c, and triglyceride was detected in 54%, 50%, and 13% of women with GDM 6 to 12 weeks postpartum, respectively, using Australian recommended standards (35).

5.4. Comparison of Our Findings with the Existing Literature: Similarities and Differences Findings

In the present study, in spite of higher level of lipid components in women with gestational diabetes, there was no significant differences in overall prevalence rate of dyslipidemia (73.3% in women with gestational diabetes compared to 74.4% in controls), and abnormal lipids components (triglycerides $\geq$ 150, LDL-C $\geq$ 130, HDL < 50, and TC/ HDLC $\geq$ 4 between 2 groups of women with GDM and controls (Table 2). However, the rate of all components except low HDL-C was higher in women with GDM (Table 1).

Results of some previous studies showed that women with GDM are at significantly higher risk of dyslipidemia after pregnancy compared to normoglycemic women during pregnancy, but there is inconsistency in these findings (7). Carr et al. found higher prevalence of dyslipidemia (34% versus 26%) in women with the history of GDM (36). Significantly higher total cholesterol (54.5% vs. 7%) at 6 to 12 weeks postpartum was reported by Quinlivan and Danielle among Australian women with GDM compared with controls. In this report, the control group included Australian general population (35).

5.5. Impact of Pre-pregnancy Overweight and Obesity

In the present study, almost all types of lipid component abnormalities were more prevalent in overweight and obese women with or without GDM. Edwards et al. found pre-pregnancy BMI (OR = 1.7) to be one of the independent risk factors of dyslipidemia in women with gestational diabetes at 6 to 12 weeks postpartum follow-up (33). Some previous studies reported similar or lower LDL-C in none-obese women with GDM, while obese women with GDM had higher level of this component compared with controls. Obese GDM- exposed women had lower HDL-C, while there were no significant differences between HDL-C level in non-obese women with GDM and controls (7). Elevated triglyceride in combination raised LDL- cholesterol, and low HDL-C are types of dyslipidemia associated with obesity. It seems these changes in obese women are related to insulin resistance (37).

5.6. The Strength and Limitations

The relative small sample size of controls was one of the limitations of this study. Continuing sampling in future months may provide subgroup analysis. Unavailability of recorded information on pre- pregnancy lipid profile was another limitation of the study. Despite such limitations, to the best of our knowledge, this study was the first population-based prospective cohort study in Khuzestan province to follow postpartum lipid profile in women with and without gestational diabetes.

5.7. Conclusion

Our findings indicated that dyslipidemia was prevalent in glucose status during pregnancy in early postpartum. Dyslipidemia screening and oral glucose test should be done routinely for women with GDM and overweight or obese women with or without gestational diabetes.

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