

Postpartum Lipid Levels in Women with Major Depression

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Abstract

Background: Maternal plasma lipids, including total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), increase during pregnancy, remaining elevated over prepregnancy levels through the immediate postpartum period. Triglycerides decrease rapidly to prepregnancy levels after delivery. Few data on postpartum lipid levels are available, and levels in postpartum women with depression have not been evaluated. We sought to determine the cross-sectional levels of total cholesterol, LDL-C, HDL-C, and triglycerides between 1 and 14 weeks postpartum in postpartum women with DSM-4 diagnoses of major depression and determine if they are similarly elevated to published levels in other postpartum populations.

Methods: As part of screening for a randomized controlled trial comparing treatments for postpartum depression (PPD), women ($n = 120$) had postpartum fasting lipid levels determined. Linear regression models were used to assess the association between time postpartum and lipid levels. Analysis of covariance models (ANCOVA) assessed the association of baseline characteristics with lipids.

Results: Total cholesterol levels were >200 mg/dL in 45% of the sample at baseline. Mean baseline total cholesterol was 196 ± 39 mg/dL. There was an inverse linear relationship between postpartum week and total cholesterol, with cholesterol values decreasing an average of 4.5 mg/dL per week. Similarly, LDL-C and HDL-C trended down over time. Triglycerides were stable and within the normal range during the observation period.

Conclusions: Total cholesterol, HDL-C, and LDL-C are significantly elevated in the early postpartum period and do not return to <200 mg/dL until 6 weeks postpartum in women with PPD. The magnitude and duration of elevation are consistent with the sparse published data on nondepressed women.

Introduction

PREGNANCY ALTERS MATERNAL lipid metabolism. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride levels rise throughout the second and third trimester, peaking just before term at approximately 36 weeks of gestational age.¹⁻³ Previous studies⁴⁻⁶ have noted that lipid levels, except for triglycerides, remain elevated above prepregnancy values after delivery. The average duration of lipid elevation and the time of return to prepregnancy levels, if that is achieved, is not well studied. Pregnancy may permanently alter or reset the lipid profile in women. For healthy, nonpregnant women, optimal values for total cholesterol are <200 mg/dL, for LDL-C <100 mg/dL, and for HDL-C between 40 and 59 mg/dL.⁷ Elevated total cholesterol is associated with increased risk for cardiovascular disease (CVD) and early death.⁸

Multiple large, well-designed studies have conclusively shown that elevated cholesterol is an independent risk factor for coronary heart disease (CHD) and early death.^{9,10} Epidemiologic data have been used to set guidelines for optimal lipid levels, as outlined in the Adult Treatment Panel (ATP) III.⁷ These data underlie the recommendation for a target total cholesterol level ≤ 200 mg/dL.⁷ These studies excluded women who were pregnant or breastfeeding.

Postpartum depression (PPD) affects 14.5% women in the United States,¹¹ has long-lasting negative effects on parenting and child development, and is infrequently diagnosed and inadequately treated.¹² Risk factors for PPD include lower socioeconomic status, a history of prior depression, and stressful life events. Major depression is a risk factor for future CVD,^{8,13} and pregnant women with major depression are more likely to be overweight and obese.^{14,15} To our knowledge, there are no published data on postpartum lipid profiles in women with PPD; postpartum women with depression may have lipid

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levels higher than nondepressed postpartum women because of modifiable behavioral or genetic risk factors. This could, in turn, further increase their future risk for CVD and early death.

We sought to determine the cross-sectional levels of total cholesterol, LDL-C, HDL-C, and triglycerides between 1 and 14 weeks postpartum in postpartum women with DSM-4 diagnoses of major depression and determine if they are similarly elevated to published levels in other postpartum populations. Women with PPD who sought evaluation for a randomized controlled trial (RCT) comparing treatments for PPD had baseline plasma measurements, including total cholesterol, HDL-C, LDL-C, and triglyceride levels, obtained at enrollment to the clinical trial within 99 days (14.1 weeks) postpartum and analyzed to account for multiple demographic and health risk factors.

Materials and Methods

This study was reviewed and approved the University of Pittsburgh Institutional Review Board and registered at www.clinicaltrials.gov (NCT00744328). Women (n=120) were screened for the RCT. Eligible women met the inclusion criteria: aged 18–45 years, able to provide written informed consent in English, met criteria for major depressive disorder (MDD) by Structured Clinical Interview for DSM-4 Disorders (SCID) research interview,¹⁶ had normal laboratory evaluations (including thyroid, hematologic and hepatic functions, and negative urine pregnancy tests), and were within 14.1 weeks (99 days) of delivery. Participants were recruited from the community, three maternity hospitals, and physicians' offices in Western Pennsylvania. Women with psychosis were excluded. Women had to appear for evaluation between delivery and 99 days (14.1 weeks) postpartum; therefore, the baseline values are distributed though this time frame. Fasting blood was collected at the baseline assessment visit. Total cholesterol, HDL-C, LDL-C, and triglycerides were measured at a single laboratory facility using the Siemens Dimension clinical chemistry system (Deerfield, IL). Postpartum fasting lipids were measured on 120 subjects who met inclusion criteria and are included in this analysis.

Baseline characteristics, including age, ethnicity, education, marital status, and obstetric history, were obtained by interview. Infant feeding method (exclusively breastfeeding, breast milk and formula, exclusively formula feeding) was determined by participant self-report as well as feedings observed by study staff.

Summary statistics, means and standard deviations (SD) for continuous variables, and percentages for discrete variables were used to describe the sample. Linear regression models were used to assess the association between time and cholesterol levels. Separate analysis of covariance (ANCOVA) models were used to assess the association of baseline characteristics with cholesterol, HDL-C, LDL-C, and triglycerides. All multivariable results were adjusted for time since delivery.

Results

Characteristics of the sample at baseline are presented in Table 1; 61% of the sample were white, 35% African American, and 4% other. The mean age was 25.8 years. Mean gravidity was 2.6 and parity was 2.0. Prepregnancy mean body mass index (BMI) was available for 89 of 120 subjects (77%) and was 29.1 kg/m². The results are summarized in Figure 1

TABLE 1. SAMPLE CHARACTERISTICS (n=120)

Characteristic	Mean ± SD n (%) ^a
Age	25.8 ± 5.6
Ethnicity	
White	70 (61.4)
African American	40 (35.1)
Other	4 (3.7)
Education	
< High school	12 (12.6)
High school	28 (29.5)
Some college	36 (37.2)
College	15 (15.8)
Postgraduate	4 (4.2)
Marital status	
Married/partner	46 (46.9)
Single	52 (53)
Gravidity	2.6 ± 1.7
Parity	2.0 ± 1.1
BMI (prepregnancy)	29.1 ± 8.5
Completed weeks gestation	38.9 ± 1.7
Mode of delivery	
Vaginal (including operative)	67 (65.7)
Cesarean section	35 (34.3)
Infant feeding method	
Breast	29 (25.0)
Formula	68 (58.6)
Both	19 (16.4)
Pregnancy complications	
GDM	4 (3.4)
HTN	13 (11.2)
Preeclampsia	8 (6.9)
Days postpartum at baseline blood draw	47.2 ± 19.9
Baseline HDL-C (mg/dL)	50.4 ± 14.0
Baseline LDL-C (mg/dL)	125 ± 34
Baseline total cholesterol (mg/dL)	196 ± 39
Total cholesterol > 200 mg/dL	54 (45)

^aAll descriptive statistics are based on available data.

BMI, body mass index, defined as weight (kg)/height(m)²; GDM, gestational diabetes; HDL-C, high-density lipoprotein cholesterol; HTN, hypertension during pregnancy; LDL-C, low density lipoprotein cholesterol.

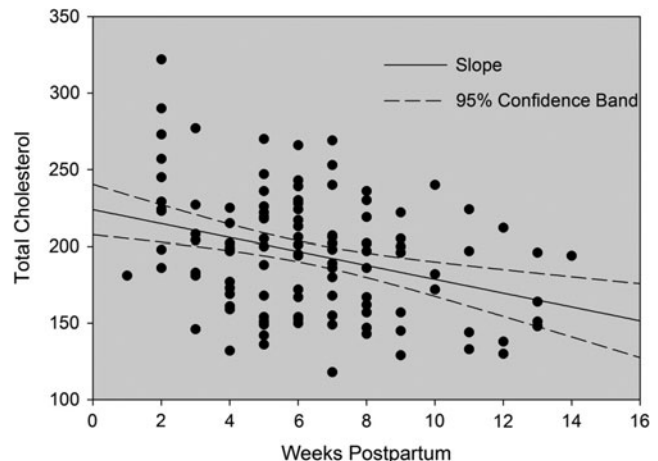


FIG. 1. Total cholesterol (mg/dL) by weeks postpartum.

TABLE 2. MULTIVARIABLE RESULTS: BETA COEFFICIENTS AND ASSOCIATED *P* VALUES BY LIPID AND MEASURE

Measure	Total cholesterol		High-density-lipoprotein cholesterol		Low-density-lipoprotein cholesterol		Triglycerides	
	coefficient ^a	p	coefficient	p	coefficient	p	coefficient	p
Age	2.0491	0.0005	0.8516	<0.0001	0.7552	0.1725	0.0095	0.3283
Race (Reference: white)		0.2568		0.0268		0.9039		0.7951
Black	-12.1145		-7.0949	0.0077	-2.8356		-0.0713	
Other	-5.7358		1.7218	0.8048	-3.1781		-0.1172	
Education level (Reference: <HS)		0.0466		0.1270		0.4090		0.1941
High school	13.6378	0.2796	3.3208		1.4485		0.3835	
Some college	29.0213	0.0175	7.7548		13.5201		0.3317	
College	19.8883	0.1597	12.2631		6.0686		0.0985	
Graduate school	54.5697	0.0098	8.3635		28.1669		0.5407	
Marital status (Reference: single)		0.5358		0.0687		0.8869		0.8994
Married/cohabiting	8.5027		4.0723		3.0658		-0.0558	
Divorced/separated	-1.1925		-8.6024		-2.2533		-0.0003	
Prepregnancy BMI	0.2806	0.5400	-0.4551	0.0048	0.3470	0.4025	0.0159	0.0309
During most recent pregnancy								
Diabetes	14.4835	0.4470	7.8184	0.2712	4.9044	0.7715	0.2418	0.4239
High BP	-14.9235	0.1680	-6.9407	0.0851	-7.9786	0.4075	0.0626	0.7178
Preeclampsia	-19.4453	0.1488	-2.9471	0.5615	-15.3994	0.1972	-0.0418	0.8464
Vaginal delivery	8.3138	0.2910	-2.2526	0.4381	9.0991	0.1872	0.1147	0.3490
Gestational age at delivery (weeks)	1.1676	0.5749	-0.2856	0.7067	1.2190	0.4962	-0.0039	0.9025
Infant feeding method (Reference: breast)		0.9931		<0.0001		0.6100		0.0004
Formula	-0.8219		-14.9185	<0.0001	7.2950		0.4790	<0.0001
Both	0.0239		-14.2676	<0.0001	4.8129		0.5100	0.0017
Parity	3.4616	0.2968	-0.6994	0.5717	1.2154	0.6846	0.0864	0.0977
Parity (Reference: 1)		0.2811		0.9966		0.4242		0.3353
2	-2.4821		0.2352		-5.2320		0.0564	
3+	11.4416		0.1953		5.2312		0.2106	
Gravidity	2.1312	0.3035	-1.0169	0.2021	0.9493	0.6069	0.0684	0.0393

All models adjusted for time since delivery.

^aFor continuous measures, such as age, the coefficient indicates the amount of change in the dependent variable (e.g., total cholesterol) for each unit increase in the dependent variable. For dichotomous measures, such as vaginal delivery, the coefficient indicates the mean difference in the dependent variable for vaginal delivery=yes compared to vaginal delivery=no. For categorical measures, such as race, the coefficient indicates the mean difference in the dependent variable for race=black compared to race=white.

BP, blood pressure; HS, high school.

and Table 2. At baseline, 45% of subjects had total cholesterol ≥ 200 mg/dL. Total cholesterol decreased linearly with week postpartum (Fig. 1). On average, total cholesterol decreased 4.5 mg/dL per week over the 14-week study period.

Older age was associated with higher total cholesterol and higher HDL-C. African American race was associated with lower HDL-C. Lower HDL-C levels also were associated with higher prepregnancy BMI and any formula feeding. Higher BMI was associated overall with a less favorable lipid profile, including higher triglycerides in addition to lower HDL-C. Triglyceride levels were higher in formula-feeding women than in exclusively breastfeeding women.

Discussion

In this cohort of 120 postpartum women with major depression, plasma lipids were observed to be elevated between 1 and 14 weeks postpartum. The very high early postpartum total cholesterol and LDL-C levels we found in postpartum women with depression are consistent with results in the sparse literature published more than three decades ago on general populations of postpartum women. In 1979, Potter and Nestel⁵ reported that plasma lipids were elevated post-

partum. They followed 43 women through pregnancy and the first year after delivery and found total cholesterol elevated at an average just above 250 mg/dL at 6 weeks and still slightly higher than prepregnancy baseline at 52 weeks. Darmody and Postle¹⁷ studied 34 women and showed a similar pattern and values for total cholesterol at approximately 250 mg/dL at 6 weeks, but they reported a return to baseline by 40 weeks.

Van Stiphout et al.⁶ compared total cholesterol and HDL-C in 831 Dutch women and reported that women who had ever been pregnant had slightly higher total cholesterol and lower HDL-C levels than similar never pregnant women. Sixty women studied from early pregnancy through 40 days postpartum by Jimenez et al.¹ showed persistently elevated total cholesterol at 40 days, with a mean of 240 mg/day. As in our study, women who breastfed had more favorable lipid profiles postpartum than had their formula-feeding peers.^{17,18} Physiologically, this is plausible, based on alterations in lipid metabolism required for lactation. It is also possible that breastfeeding is a marker for overall better health, as women who breastfeed tend to be healthier, with higher socioeconomic status and educational attainment, than formula-feeding women. The potential positive effect of breastfeeding on lipids could represent a reduction in long-term risk and is

an additional reason to promote breastfeeding to improve public health.

Both older age and higher BMI have been shown to be associated with elevated total cholesterol and LDL-C, as in our study.¹⁹ Although African Americans have higher rates of CVD, race has not been consistently shown to be associated with differences in lipid profiles.²⁰ Previous studies of postpartum lipids have shown no association with maternal age^{1,5,17,18,21} or weight.^{1,17,21} Several studies, however, either did not examine these covariants, did not report their significance, or only examined them in relation to change in lipids over time rather than for absolute lipid levels. Because of this, as well as the multiethnic nature of our sample and the increasing rate of obesity in the United States since some of the older studies were published, it is difficult to accurately compare these results.

HDL-C has been studied more recently. In two published reports from the Coronary Artery Risk Development in Young Adults (CARDIA) study,^{21,22} postpartum HDL-C was found to be decreased compared to prepregnancy levels for a period of 10 years after the first pregnancy, consistent with van Stiphout's findings.⁶ This is suggestive of long-term lipid alterations produced by pregnancy.

The strengths of this study include the relatively large sample of postpartum women who provided standardized, fasting measures of plasma lipids done in the same laboratory. Laboratory assessments for thyroid function, complete blood count (CBC), full metabolic screens, and detailed information on breastfeeding status were available for all participants. The data (Fig. 1) provide a visual representation of the decline in total cholesterol by postpartum week to aid interpretation of laboratory values obtained in postpartum women. We established the average time of return of cholesterol to the desired value of <200 mg/dL to be 6 weeks after birth. Study participants were recruited from a diverse community, which increases generalizability. Finally, PPD was diagnosed objectively with DSM-4 diagnostic interviews.

Although the sample size allows a reasonable evaluation of postpartum lipids, it is too small to identify contributions from pregnancy complications, such as preeclampsia or gestational diabetes. Likewise, it would be preferable to have prepregnancy BMI on all subjects, and some are missing from this sample. Because of methodologic differences, we are unable to directly compare the results from our depressed population with the populations previously studied. Finally, prepregnancy lipid levels for comparison would allow us to make interperson comparisons that we are unable to do with our current data.

The possible long-term effects of elevated postpartum lipids on health, including potential interaction with depression as well as cardiovascular health, are an area for further study. In depressed patients, lipoprotein structure is changed toward increasing LDL-C and higher atherogenic potential, and remission is associated with improvement of the LDL-C/HDL-C ratio.²³ Longitudinal assessment to determine if subgroups of postpartum women at risk (such as those with depression) have sustained serum cholesterol elevations are also needed. The women in this RCT will be evaluated for lipid profiles related to both treatment assignment and remission status at study completion. People with severe mental illness, including refractory depression, are at increased risk of early

death.²⁴ Women with depression are more likely to be obese and may already be at increased risk of death from CVD. Additional studies on the effects of reproductive life, including pregnancy and lactation, are required to understand the cumulative burden of risk factors throughout life and their role in future health. This study is the first step in understanding whether physiologic changes in lipid metabolism caused by pregnancy may affect long-term health outcomes in women with depression.

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