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Serum cholesterol levels and mood symptoms in the postpartum period

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Abstract

During pregnancy, the total serum cholesterol concentration rises up to 43%, followed by a rapid fall after delivery. Mild depressive symptoms ('postpartum blues') are a common complication of the puerperium and affect 30–85% of women in the early postpartum period. Based on these observations, it has been suggested that the sudden fall in cholesterol levels after delivery could serve as a 'natural model' to test the suggested association between cholesterol and mood. The present study was designed to expand the database concerning the association between cholesterol levels and mood in the postpartum period and to address some methodological problems raised by previous studies. Forty-seven healthy primiparous women were interviewed with a structured clinical interview on two occasions: during late pregnancy (median: day −20 before the expected delivery) and during the early postpartum period (median: day 32 after delivery). On both occasions, serum concentrations of total and HDL cholesterol were measured and mood symptoms were assessed with the state form of Spielberger's State-Trait Anxiety Index (STAI), the state form of the State-Trait Anger Scale (STAS), and the Beck Depression Inventory (BDI). We found significant, albeit moderate, relationships between serum cholesterol levels and mood symptoms in the postpartum period that were not present during late pregnancy. Lower postpartum levels of total cholesterol were associated with symptoms of anxiety ($r=-0.30$, $P=0.04$), anger/hostility ($r=-0.31$, $P=0.04$), and depression ($r=-0.35$, $P=0.02$), and lower postpartum levels of HDL cholesterol were associated with symptoms of anxiety ($r=-0.34$, $P=0.02$). This study confirms that the physiological fall in blood lipids in the postpartum period can be a useful model to test the relationship between serum cholesterol levels and mood.

Keywords: Depression; Anxiety; Anger; Hostility; Pregnancy; Puerperium; Cholesterol

1. Introduction

Debate has been ongoing in the field of psychiatric research regarding the possible relevance of cholesterol to mental health (Wardle, 1985; Boston et al., 1996). Associations between low serum cholesterol concentrations and depressive symptoms have been found in different populations (Horsten et al., 1997; Maes et al., 1999; Steegmans

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et al., 2000; Troisi et al., 2001), but other studies have yielded negative findings (Freedman et al., 1995). The data to support a relationship between cholesterol and aggression are also divided (Apter et al., 1999; New et al., 1999), even though, in a recent review, Golomb (1998) concluded that the evidence in the literature is consistent with a causal connection between low or lowered cholesterol levels and violence. In line with these clinical data, experimental studies in non-human primates have shown that monkeys on a low fat/low cholesterol diet (and having lower mean serum cholesterol than a high fat/high cholesterol group) are more likely to engage in aggressive behavior (Kaplan et al., 1994, 1997).

The association between low cholesterol and negative mood has been explained tentatively on the basis of hypothesized neurobiological mechanisms linking serum cholesterol to brain function. Total cholesterol and its major constituents, including HDL, LDL and VLDL cholesterol, have many neurobiological roles (Wood et al., 1999) and may influence mood through modification of neuronal membranes; myelin; enzyme function; absorption and transport of fat-soluble vitamins and toxins; and steroid hormones and through effects on production, reuptake, or metabolism of neurotransmitters. In particular, there is evidence that low or lowered cholesterol levels may be associated with reduced central serotonin activity (Buydens-Branchey et al., 2000).

During pregnancy, the total serum cholesterol concentration rises up to 43%, reaching in the third trimester values around 9.83 mmol/l (Piechota and Staszewski, 1992). These values undergo a rapid fall after delivery and normalize by the 20th week postpartum (van Stiphout et al., 1987). Mild depressive symptoms ('postpartum blues') are a common complication of the puerperium and affect 30–85% of women in the early postpartum period (Nonacs and Cohen, 2000). Based on these observations, it has been suggested that the sudden fall in cholesterol levels after delivery could serve as a 'natural model' to test the association between cholesterol and mood (Ploeckinger et al., 1996).

So far, only two studies (Ploeckinger et al., 1996; van Dam et al., 1999) have analyzed the relationship between serum cholesterol levels and mood in the postpartum period. These two studies have yielded conflicting results. In a sample of 20 healthy primiparous women, Ploeckinger et al. (1996) found a significant correlation between self-rated depressive symptoms and relative changes in cholesterol levels from prepartum (day 14 before the expected delivery) to postpartum (day 4 after delivery). In a study of 266 Dutch women, van Dam et al. (1999) found that the decline in serum cholesterol between week 32 of pregnancy and week 10 postpartum was similar for women who became depressed in the subsequent period and women who did not.

The present study was designed to expand the database concerning the association between cholesterol levels and mood in the postpartum period and to address some methodological problems raised by the studies cited above. First, unlike the studies by Ploeckinger et al. (1996) and van Dam et al. (1999), we did not limit mood assessment to the measurement of depression. Since postpartum mood disturbance includes a variety of symptoms, we measured anxiety and anger/hostility in addition to depression. Second, we varied the time of assessment across the participants to include both women in the last days before delivery (unlike the study by van Dam et al., 1999) and women in the 1st and 2nd months postpartum (unlike the study by Ploeckinger et al., 1996). Serum cholesterol concentration has been shown

Table 1
Serum cholesterol concentrations and mood scores (mean ± S.D.) for 47 healthy primiparous women at prepartum (median day before delivery: −20) and postpartum (median day after delivery: 32)

	Prepartum	Postpartum
Total cholesterol (mg/dl)	290.91 ± 44.40[a]	235.19 ± 43.69[a]
HDL cholesterol (mg/dl)	71.13 ± 17.97[a]	62.75 ± 13.78[b]
STAI	33.30 ± 7.41[a]	33.85 ± 8.45[c]
STAS	15.67 ± 2.83[a]	16.25 ± 3.18[c]
BDI	7.32 ± 3.13[c]	6.64 ± 5.10[c]

Different sample sizes reflect missing data. STAI, state form of Spielberger's State-Trait Anxiety Index; STAS, state form of the State-Trait Anger Scale; BDI, Beck Depression Inventory.

[a] $N = 46$.

[b] $N = 45$.

[c] $N = 47$.

to peak in the last days of pregnancy (Potter and Nestel, 1979) and, in some women, postpartum mood disturbance emerges not in the days immediately after delivery but some weeks later (Nonacs and Cohen, 2000).

2. Methods

2.1. Participants

Between January 1997 and March 1998, 74 pregnant women who were nulliparous and registered consecutively for obstetric care were invited to participate in this study. Fifty-three were willing to participate (response rate 72%). We excluded four women with metabolic disorders, gestosis or fetal complications and two women who had a history of anxiety and/or a depressive disorder. As a result, this report consists of 47 healthy primiparous women (age: mean 29.4 years, S.D. 3.8, range 23–39; education: mean 12.9 years, S.D. 3.1, range 8–19). All the women, except three, were breast-feeding when evaluated in the postpartum period. None of the women used cholesterol-lowering medication or psychotropic drugs. Written consent of the participants, as well as the approval by the university ethics committee, was obtained.

2.2. Data collection

Participants were interviewed by the same psychiatrist with a structured clinical interview (SCID) (Spitzer et al., 1987) on two occasions: during late pregnancy (median: day −20 before the expected delivery, range: day −52 to −1) and during the early postpartum period (median: day 32 after delivery, range: day 16–56). During the first interview, marital stress and socioeconomic problems were assessed by standard questions. One woman was unmarried; all others were married or had a partner. None of the women reported substantial marital or financial problems.

On both occasions, biochemical and psychometric data were collected. Blood was collected between 08:00 and 09:00 h following an overnight fast. Serum concentrations of total cholesterol and high-density lipoprotein (HDL) cholesterol were measured. Mood was assessed with the state form of Spielberger's State-Trait Anxiety Index (STAI) (Spielberger et al., 1983a), the state form of the State-Trait Anger Scale (STAS) (Spielberger et al., 1983b), and the Beck Depression Inventory (BDI) (Beck and Steer, 1987).

2.3. Statistical analysis

Prepartum and postpartum cholesterol concentrations and mood scores were compared using *t*-tests for paired samples. We calculated Pearson correlation coefficients between mood scores and absolute cholesterol concentrations and relative change in total cholesterol levels (from prepartum to postpartum values, expressed as a percentage of the initial concentration). The days of prepartum and postpartum assessments varied widely across the women of this study. In order to control for the possible confounding effect of such a variation, we conducted two different types of statistical analyses. First, we calculated partial correlations between mood scores and cholesterol concentrations after adjustment for the day of assessment. Second, we calculated a test of homogeneity of the regression slopes through the factor by regressor interaction effect in an analysis of covariance (ANCOVA) model (Stevens, 1996).

3. Results

At the prepartum and postpartum interviews, none of the participants met DSM-III-R criteria for a diagnosis of major depressive disorder. The number of participants with clinically significant depressive symptoms (defined by a BDI total score ≥ 15) was one at the prepartum interview and four at the postpartum interview. Mood scores did not change significantly from prepartum to postpartum (STAI: $t=-0.49$, d.f.$=45$, $P=0.62$; STAS: $t=-1.60$, d.f.$=45$, $P=0.11$; BDI: $t=1.06$, d.f.$=46$, $P=0.29$). As expected, there was a marked decrease in cholesterol concentrations between the first measurement during late pregnancy and the second measurement during early postpartum (total cholesterol: $t=9.11$, d.f.$=44$, $P<0.0001$; HDL cholesterol: $t=4.93$, d.f.$=43$, $P<0.0001$) (Table 1).

Prepartum total and HDL cholesterol concentrations were not significantly correlated with mood scores (total cholesterol: STAI, $r=0.03$, $N=45$, $P=0.83$; STAS, $r=-0.25$, $N=45$, $P=0.09$; BDI, $r=-0.19$, $N=46$, $P=0.21$; HDL cholesterol: STAI, $r=-0.14$, $N=45$, $P=0.37$; STAS, $r=-0.14$, $N=45$, $P=0.35$; BDI, $r=-0.26$, $N=46$, $P=0.08$). The analysis based on partial correlations controlling for the day of assessment before delivery yielded similar results (total cholesterol: STAI, $r=-0.04$, d.f.$=42$, $P=0.77$; STAS, $r=-0.28$, d.f.$=42$, $P=0.07$; BDI, $r=-0.19$, d.f.$=42$, $P=0.21$; HDL cholesterol: STAI, $r=-0.15$, d.f.$=42$, $P=0.33$; STAS, $r=-0.16$, d.f.$=42$, $P=0.28$; BDI, $r=-0.29$, d.f.$=42$, $P=0.053$).

Postpartum total cholesterol concentrations were significantly and negatively correlated with mood scores (STAI, $r=-0.30$, $N=46$, $P=0.04$; STAS, $r=-0.31$, $N=46$, $P=0.04$; BDI, $r=-0.35$, $N=46$, $P=0.02$) (Fig. 1). Postpartum HDL cholesterol concentrations showed no significant correlations with the STAS ($r=-0.26$, $N=45$, $P=0.08$) and the BDI ($r=0.25$, $N=45$, $P=0.09$). However, there was a significant negative correlation between the postpartum HDL cholesterol concentrations and anxiety symptoms as measured by the STAI ($r=-0.34$, $N=45$, $P=0.02$). These significant associations remained after adjustment for the day of assessment after delivery (total cholesterol: STAI, $r=-0.29$, d.f.$=43$, $P=0.05$; STAS, $r=-0.30$, d.f.$=43$, $P=0.05$; BDI, $r=-0.34$, d.f.$=43$, $P=0.02$; HDL cholesterol: STAI, $r=-0.34$, d.f.$=42$, $P=0.02$; STAS, $r=-0.26$, d.f.$=42$, $P=0.09$; BDI, $r=-0.25$, d.f.$=42$, $P=0.10$).

In addition to partial correlations, we calculated a test of homogeneity of the regression slopes to exclude that the relationship between postpartum cholesterol and mood symptoms varied with the time following delivery in which the women were evaluated. Based on the time of assessment, the sample was divided into two subgroups (women evaluated during the 1st month postpartum, $N=21$; women evaluated during the 2nd month postpartum, $N=26$). The formal significance of the test was calculated through the factor by regressor interaction effect in an ANCOVA model (factor: time of assessment; regressor: cholesterol; dependent: psychometric scale). The Time of Assessment×Total Cholesterol interaction effect was not significant for the STAI ($F=0.64$, d.f.$=1, 42$, $P=0.43$), the STAS ($F=2.39$, d.f.$=1, 42$, $P=0.13$),

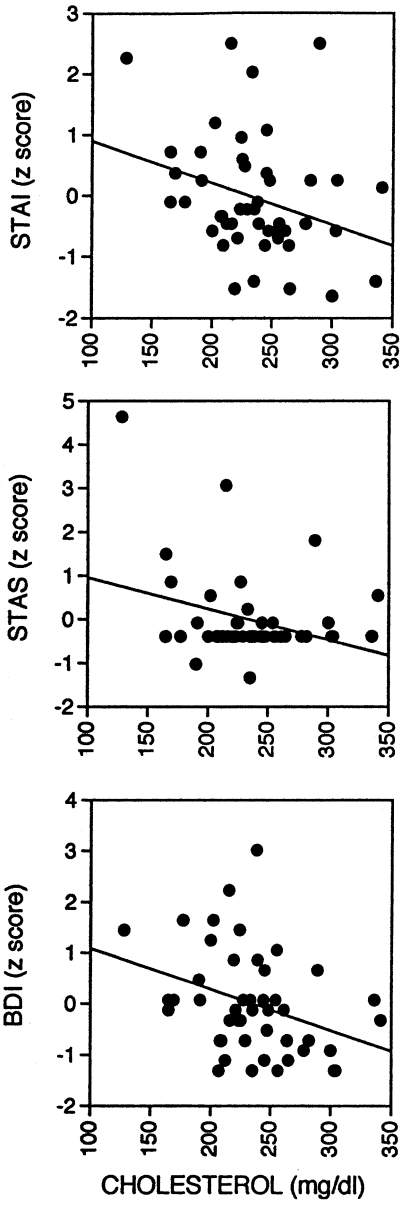

Fig. 1. Correlation between serum concentrations of total cholesterol and scores on the state form of the STAI, the state form of the STAS, and the BDI in 47 healthy primiparous women during the early postpartum period (median day after delivery: 32).

and the BDI ($F=0.73$, d.f.$=1, 42$, $P=0.40$). Similarly, the Time of Assessment×HDL Cholesterol interaction effect was not significant for the STAI ($F=1.94$, d.f.$=1, 41$, $P=0.17$), the STAS ($F=1.87$, d.f.$=1, 41$, $P=0.18$), and the BDI ($F=0.75$, d.f.$=1, 41$, $P=0.78$). Based on these results, we can conclude that, in our sample, the time of assessment did not influence the relationship between postpartum cholesterol levels and mood symptoms.

The relative decrease in total cholesterol levels from prepartum to postpartum was not correlated with postpartum mood scores (STAI, $r=-0.16$, $N=45$, $P=0.30$; STAS, $r=-0.12$, $N=45$, $P=0.43$; BDI, $r=-0.27$, $N=45$, $P=0.08$). The analysis based on partial correlations controlling for the day of assessment after delivery yielded similar results (STAI, $r=0.15$, d.f.$=42$, $P=0.33$; STAS, $r=-0.09$, d.f.$=42$, $P=0.56$; BDI, $r=-0.26$, d.f.$=42$, $P=0.08$).

4. Discussion

These results provide evidence for significant, albeit moderate, relationships between serum cholesterol levels and mood symptoms in the postpartum period that are not present during late pregnancy. In our sample of 47 healthy primiparous women, lower postpartum levels of total cholesterol were associated with symptoms of anxiety, anger/hostility, and depression, and lower postpartum levels of HDL cholesterol were associated with symptoms of anxiety.

A comparison of our results with those of previous studies requires a preliminary discussion of the current classification of postpartum mood disorders. Postpartum non-psychotic psychiatric illness is typically divided into two categories: postpartum blues and postpartum depression. Postpartum blues is a self-limiting syndrome that usually begins on the second or third day postpartum, peaks on the 5th to 7th day, and should start to remit by the 2nd week. Occasionally, an extended period of the blues will continue into the 4th and 5th weeks postpartum. About 25% of women with blues will go on to develop postpartum depression (Sichel, 2000). The signs and symptoms of postpartum depression are generally indistinguishable from those characteristic of major depression. While some women report the acute onset of symptoms shortly after delivery, postpartum depression more commonly develops insidiously over the first 6 postpartum months. Although postpartum blues and postpartum depression vary in severity, it is not clear if they actually represent two distinct disorders (Nonacs and Cohen, 2000).

Among the women of this study, none qualified for a DSM-III-R diagnosis of major depression. The absence in our sample of well-documented risk factors for postpartum depression can explain such an unusual finding. We excluded women with a personal history of anxiety and/or depressive disorder, and none of the women had substantial marital and/or financial problems. The five women with a BDI total score ≥ 15 (one in the prepartum and four in the postpartum) had many of the neurovegetative signs and symptoms (i.e. sleep and appetite disturbance, diminished libido, low energy) characteristic of major depression, but they did not meet DSM-III-R criterion A for a diagnosis of major depression (i.e. either depressed mood or loss of interest or pleasure for a period of at least 2 weeks).

Differences in inclusion criteria and diagnostic assessment preclude a direct comparison between our results and those of van Dam et al. (1999), who found that the decline in serum cholesterol between week 32 of pregnancy and week 10 postpartum was similar for women who became depressed in the subsequent period and women who did not. First, unlike the sample studied by van Dam et al., our sample did not include multiparous women and women with a personal history of anxiety and/or depressive disorder. Second, to detect the presence of mood disturbance, we used both a dimensional instrument (the BDI) and categorical criteria (the DSM-III-R diagnosis) whereas van Dam et al. (1999) limited their clinical assessment to the use of the categorical Research Diagnostic Criteria. However, our results are in line with those of the study by Ploeckinger et al. (1996), who employed a dimensional instrument (the Zung Self-Rating Depression Scale) and observed a significant correlation between postpar-

tum cholesterol decline and depressive symptoms in a sample of 20 healthy primiparous women.

In most studies of the association between cholesterol and psychological variables, levels of total cholesterol were examined and not those of the HDL and LDL fractions. A few studies assessed HDL and LDL cholesterol levels in addition to total cholesterol. Buydens-Branchey et al. (2000) found, in a sample of personality-disordered cocaine addicts withdrawn from cocaine, that patients who had a past history of aggression had significantly lower levels of HDL cholesterol. Maes et al. (1999) found significantly lower serum HDL cholesterol levels in depressed patients compared with control subjects. They also observed that total cholesterol was lower in the patients but that the differences between patients and controls was less marked. These data led Maes et al. to speculate that the most important change in serum lipid composition in depressed subjects could occur in HDL cholesterol rather than in total cholesterol. In the present study, we found an association between postpartum HDL cholesterol and symptoms of anxiety. However, total cholesterol emerged as a stronger correlate of postpartum mood symptoms than HDL cholesterol.

We did not control for postpartum hormonal changes. A rapid decline in progesterone and estrogen concentrations occurs within days after delivery (Hendrick et al., 1998), and concentrations of these hormones are positively associated with cholesterol concentrations during pregnancy (Montelongo et al., 1992). Therefore, we cannot exclude that correction for postpartum hormone decline would attenuate the observed association between postpartum cholesterol concentrations and mood symptoms. However, it is worth noting that the significant correlations between postpartum decrease in cholesterol and depressive symptoms found by Ploeckinger et al. (1996) remained even after adjustment for progesterone concentration.

Our results must be considered with caution because of the small sample size, the exclusion of multiparous women and women with a personal history of anxiety and/or depressive disorder, and the lack of control for postpartum hormonal changes. However, they provide further evidence for the hypothesis that the physiological fall in blood lipids in the postpartum period can be used as a natural model to test the relationship between serum cholesterol levels and mood.

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