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Normal cholesterol levels in the immediate postpartum period: A risk factor for depressive and anxiety symptoms?

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ABSTRACT

We aimed to ascertain if cholesterol levels within the reference standards for healthy non-pregnant women are a risk factor for depressive and anxiety symptoms in the immediate postpartum period. During the first week after delivery, total cholesterol levels of 120 new mothers were measured and their mood state was assessed with the Profile of Mood States (POMS). Two weeks before delivery, mothers' personal and family history of mood disturbances was assessed with the Maternal History of Mood Disturbances (MHMD) scale. Only 26 (22%) of the new mothers had normal cholesterol levels (≤ 200 mg/dL). Mothers with normal levels did not differ on psychometric measures from those with high levels. However, in the subgroup of mothers with normal cholesterol, those with lower levels experienced more symptoms of anxiety, depression and fatigue and scored higher on the MHMD scale. In the larger group of mothers with high cholesterol levels, history of mood disturbances and postpartum depressive and anxiety symptoms were not correlated with total cholesterol. Measuring cholesterol levels in the peripartum can be useful to identify a subgroup of women with naturally low cholesterol levels and an increased risk for postpartum depressive and anxiety symptoms.

1. Introduction

The spectrum of mood disturbances affecting postpartum women includes postpartum blues, postpartum depression, and postpartum psychosis (Norhayati et al., 2015). Postpartum blues occurs in 50–85% of women following delivery. It peaks around the fourth day and resolves by the tenth day following delivery. Symptoms include brief crying spells, anxiety, sadness, poor sleep, confusion, and irritability. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (American Psychiatric Association, 2013) defines postpartum depression as a depressive episode with moderate to severe severity that begins four weeks after delivery. Clinical manifestations of postpartum depression include inability to sleep or sleeping much, mood swings, change in appetite, fear of harming, extreme concern and worry about the baby, sadness or excessive crying, feeling of doubt, guilt and helplessness, difficulty concentrating and remembering, loss of interest in hobbies and usual activities, and recurrent thoughts of death, which may include suicidal ideation. Most reports indicate that 10–15% of new mothers experience postpartum depression, with the most recent meta-analysis estimating the prevalence within three months after delivery at 19.2% for minor and 7.1% for major postpartum depression (Gavin et al., 2005). Postpartum psychosis is rare, with a prevalence of

0.1–0.2%. Symptoms may include restlessness, agitation, sleep disturbance, paranoia, disorganized thoughts, impulsivity, hallucinations, and delusions. It peaks in the first two weeks after delivery and is more common in new mothers aged 35 years and above.

A large body of empirical studies have examined risk factors for mood disturbances affecting postpartum women (Yim et al., 2015). Current evidence can be categorized into two categories, biological (e.g., genetic factors, physiological changes related to the endocrine system or the immune system) (e.g., Skalkidou et al., 2012) and psychosocial (e.g., the quality of mothers' interpersonal relationships, perceived and received social support, maternal attachment style) (Dennis and Hodnett, 2007). In the present study, we focused on one biological risk factor that has been scarcely investigated in new mothers: cholesterol levels in the immediate postpartum period.

Studies of the relationship between cholesterol levels and postpartum mood symptoms fall within the more general research area of the relationship between serum cholesterol and psychiatric morbidity (Troisi, 2009). A large body of empirical studies have linked low cholesterol levels with psychiatric symptoms or behavioral disorders including aggression (e.g., Eriksen et al., 2017), suicide and self-harm (e.g., Wu et al., 2016), impulsivity (e.g., Tomson-Johanson and Harro, 2018), depression (e.g., You et al., 2013), and cognitive

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dysfunction (e.g., Leritz et al., 2016). It is worth noting that the relationship between cholesterol levels and mental health is nonlinear and emerges only when the statistical analysis focuses on subjects with low levels of cholesterol (Boscarino et al., 2009; Pozzi et al., 2003; Troisi, 2011). This finding inspired the research design of the present study that focused on a subgroup of postpartum women with unusual low levels of cholesterol.

Lipid parameters, including total cholesterol, have been shown to be elevated in pregnancy (Bartels and O'Donoghue, 2011; Lippi et al., 2007). Cholesterol levels rise progressively from the 1st to the 3rd trimester and undergo a rapid fall in the early postpartum period, though still remaining outside non-pregnant ranges. 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 low cholesterol and mood disturbances found in other clinical populations (Ploeckinger et al., 1996). In a previous study of 47 healthy primiparous women assessed in the early postpartum period with a structured clinical interview and self-reported symptom scales, Troisi et al. (2002) found that lower levels of total cholesterol were significantly correlated with symptoms of anxiety, anger/hostility, and depression. Other studies that have analyzed the relation between cholesterol and mood in the postpartum period have yielded negative results (Grussu et al., 2007; van Dam et al., 1999). In their epidemiological study including 34,653 participants, Tebeka et al. (2016) reported an association between hypercholesterolemia and perinatal depression (adjusted odd ratio: 3.98). However, the diagnosis of hypercholesterolemia was retrospective (past 12 months) and based on two questions ("did you have hypercholesterolemia?"; "did a doctor confirm the diagnosis?").

Studies of cholesterol and mood in the postpartum period have major clinical implications for women's mental and physical health. In the general population, total cholesterol levels above 200 mg/dL (circa 5.0 mmol/L) are associated with a higher risk of cardiovascular disease (Catapano et al., 2016), and the majority of pregnant women have a total cholesterol level above this (Prairie et al., 2012). Hypercholesterolemia is not treated in pregnancy, partly due to the absence of normal parameters for pregnancy, as well as clinicians' uncertainty as to the significance of elevated levels for a limited time (Bartels et al., 2012). Clearly, the relationship between cholesterol levels and mood disturbances is one of the variables to be considered in the calculation of the cost/benefit ratio of cholesterol-lowering interventions in pregnant and postpartum women. In this study, we addressed one aspect of this clinical problem by ascertaining if cholesterol levels within the reference standards for the healthy non-pregnant population are a risk factor for depressive and anxiety symptoms in the immediate postpartum period.

2. Method

2.1. Participants

This study was based on a convenience sample recruited in a public hospital. Pregnant women were considered for participation if they were medically healthy (including no treatment with lipid-lowering drugs) and had a singleton uncomplicated pregnancy. The possible presence of psychiatric lifetime diagnoses was not investigated. Of 132 invited pregnant women fulfilling inclusion criteria, 120 accepted to participate (refusal rate: 9%) and were enrolled between February and October 2002. All these new mothers were born in Italy (mean age: 29.92 years; range: 20–40 years) and had a vaginal full term delivery (between 39 weeks and 40 weeks 6 days). Most of them were multiparous (96%) and were co-living with the father of the newborn (87%). The mothers completed psychometric assessment at two time points: two weeks before delivery (personal and family history of mood disturbances) and during the first week after delivery (mood state) with no lost to follow-up. Mothers' personal and family history of mood

Table 1
Maternal History of Mood Disturbances (MHMD) scale.

1. Is there a family member who has or has had mood or emotional problems, problems with anxiety, or abuses alcohol (note, these conditions are often untreated)?
2. Have you ever experienced periods of sad or low mood, or lost interest in your usual activities?
3. If yes, were there changes in your sleep, appetite or concentration?
4. Have you ever thought about harming yourself, or have you attempted to harm yourself?
5. Have you at any time of your life believed that you have experienced depression, even though it has resolved on its own or while you have received counseling?
6. Did you have difficulties coping and feeling like your usual self for any length of time following a previous birth of one of your children?
7. Is there evidence for a previous postpartum depression?
8. Have you ever had medications prescribed for anxiety or depression?
Scoring, no = 0, yes = 1; possible score = 0–8

disturbances was assessed before delivery to avoid the confounding impact of postpartum symptoms. The research protocol was approved by the ethical committee of the recruiting public hospital. Women were given verbal and written explanations of the study. Signed consent forms were obtained from each woman before participation.

2.2. Measures

2.2.1. History of mood disturbances

We used the Maternal History of Mood Disturbances (MHMD) scale to assess mothers' personal and family history of mood disturbances (Cronbach's alpha: median value of 0.88). The scale is based on a yes/no response format with a total score ranging from 0 to 8 (Table 1). The eight questions included in the scale were originally proposed by Sichel (2000) to assess the risk of postpartum mood disorders. In a previous study conducted in this sample of new mothers (Croce Nanni and Troisi, 2017), we showed that the MHMD scale was a significant predictor of anxiety and depressive symptoms in the immediate postpartum period.

2.2.2. Postpartum depressive and anxiety symptoms

Each new mother compiled the self-administered state version of the Profile of Mood States (POMS) asking her to describe "how you have been feeling today." The POMS was administered on the day of discharge (median: 4th day). The POMS is a 65-item, adjective-rating scale designed to measure subjective mood states where respondents are presented with a list of feelings (McNair et al., 2000). Each question is rated on a 5-point Likert-type scale ranging from 0 (not at all) to 4 (extremely). Total mood disturbance is calculated by subtracting the Vigor scale score from the sum of the Anxiety, Depression, Anger, Fatigue, and Confusion (reflecting bewilderment and uncertainty) scale scores. The POMS has excellent psychometric properties with coefficients alpha ranging from 0.77 (Confusion) to 0.92 (Depression) (median value of 0.89) (Weiner et al., 2012). A previous study of postpartum women reported that a score of 20 or higher on the POMS depression scale may indicate the presence of clinically significant depressive symptoms (Groer and Vaughan, 2013). The POMS has been incorporated in a number of studies with postpartum women (e.g., Fisher et al., 2002; Hayes et al., 2001).

2.2.3. Cholesterol levels

Cholesterol levels were measured within the first week postpartum. Blood samples (5 ml) were drawn by a trained physician between 07:30 and 08:30 am after the participants had fasted for at least 12 h. Samples were immediately delivered to the hospital laboratory and analyzed for total cholesterol. On the same day when fasting plasma sample was collected, each participant completed the POMS.