

Association of Serum Lipid Profiles with Depressive and Anxiety Disorders in Menopausal Women

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Background: Several studies have investigated the relationships of lipid levels with depressive and anxiety disorders, and their results revealed an association between low cholesterol and higher levels of depressive symptoms in young, middle-aged, and postpartum women. However, few studies have explored this relationship in menopausal women. Hence, in this study of menopausal Taiwanese women, we attempted to determine the correlation of depressive and anxiety disorders with serum lipid profiles.

Methods: This was a cross-sectional study covering a 2-year period. Sixty-nine menopausal women who visited the gynecologic outpatient department of our hospital were enrolled. Psychiatric diagnoses were made using the semi-structured clinical interview for the Diagnostic and Statistical Manual (DSM-IV) criteria. Blood samples for serum lipid profiles were simultaneously collected. Data were analyzed using analysis of co-variance (ANCOVA) adjusted for age and body mass index (BMI).

Results: Total cholesterol (TC) and low-density lipoprotein (LDL) were higher in postmenopausal women than in perimenopausal women, but this was not true for triglyceride (TG), high-density lipoprotein (HDL), very-low-density lipoprotein (VLDL), the TC/HDL ratio, or the LDL/HDL ratio. However, when peri- and postmenopausal women were categorized into normal controls and those having anxiety disorders and depressive disorders, no significant differences were found in lipid concentrations of TG, TC, HDL, VLDL, LDL, TC/HDL, or LDL/HDL among the 3 groups.

Conclusions: Although these results do not suggest that serum lipid profiles can be used as biological markers to distinguish depressive or anxiety disorders in menopausal women, larger samples are required to prove such results in the future.

(*Chang Gung Med J* 2006;29:325-30)

Key words: depression, anxiety, cholesterol, menopause, lipids.

Several studies have investigated relationships of lipid levels with depressive or anxiety disorders.⁽¹⁻⁶⁾ Possible explanations can be derived from several studies that showed how depression may have a biological link to low cholesterol by its asso-

ciation with altered central serotonergic functions.⁽⁷⁻⁹⁾ On the other hand, some studies also showed either no such association,^(10,11) or yielded inconsistent results,^(12,13) especially studies including both male and female participants.

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Depression occurs about 2 times more frequently in women than in men,⁽¹⁴⁾ and may increase during times of menopause.^(15,16) Most cross-sectional studies suggest that perimenopausal women are more likely to report depressive symptoms than pre- or postmenopausal women.^(17,18) Several studies also revealed an association between low cholesterol and higher levels of depressive symptoms in young,⁽⁴⁾ middle-aged,⁽¹⁹⁾ and postpartum women.⁽²⁰⁾ However, few studies have focused on exploring the association of depressive and anxiety disorders with serum lipid profiles in menopausal women.

As in Western countries, depressive and anxiety disorders are diagnosed more frequently in women than in men in both China and Taiwan.⁽²¹⁻²³⁾ However, most women with depressive or anxiety disorders are seen in general medical rather than mental health settings.^(24,25) So, relatively few psychiatric studies have focused on menopausal women.

The purpose of this study was to determine the correlation of depressive and anxiety disorders with serum lipid profiles of menopausal Taiwanese women.

METHODS

Subjects and design

This cross-sectional study was carried out from September 2001 to June 2003 at Chang Gung Memorial Hospital in Kaohsiung, a large medical center located in southern Taiwan.

The original sample consisted of 90 menopausal women who visited the gynecologic outpatient department for complaints of climacteric symptoms. They were invited to undergo further psychiatric counseling. Fifteen women were excluded due to a missing fasting blood sample, while 6 were excluded for a concurrent major medical illness, such as cardiovascular, renal, or hepatic disease, or alcoholism or substance abuse. Thus, the final sample included 69 women. None was using medication for hypercholesterolemia during the study period.

The menopausal stage was divided into perimenopausal (i.e., the period in which clinical features of approaching menopause commence until the end of the first year after menopause) and postmenopausal status (i.e., no menstrual period for at least 1 year).⁽²⁶⁾ All of the participants provided signed informed consent after receiving a full expla-

nation of the study.

All of the subjects were assessed by the same psychiatrist according to a semi-structured clinical interview for the criteria of the Diagnostic and Statistical Manual of Mental Disorder, fourth edition (DSM-IV) (American Psychiatric Association, 1994). All were categorized into either normal controls (with no definite psychiatric diagnosis) or as having anxiety disorders or depressive disorders. Another grouping included normal controls and those with panic disorder, mixed anxiety-depressive disorder, dysthymic disorder, and major depressive disorder.

Laboratory data

Serum lipid and lipoprotein concentrations, including triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and the ratios of TC/HDL and LDL/HDL, were measured using enzymatic determinations (CHOD/PAP, Boehringer Mannheim, Mannheim, Germany) after fasting for at least 9 h on the morning following psychiatric counseling.⁽²⁷⁾

Statistical analysis

Participants were grouped according to different diagnostic categories according to either symptoms or specific disorders. Data analysis was performed using analysis of co-variance (ANCOVA) after age and body mass index (BMI) had been adjusted for using group mean differences for the different groups. A value of $p < 0.05$ was considered statistically significant.

RESULTS

The demographic data, peri- or postmenopausal status, and serum lipid levels of the 69 women are shown in Table 1. From the point of view of the menopausal stage, the women were grouped into 2 categories: perimenopausal status ($n = 41$), and postmenopausal status ($n = 28$). Using ANCOVA adjusted for age, there were significant differences in serum concentrations of TC ($F = 7.226$, $p = 0.009$) and LDL ($F = 5.833$, $p = 0.019$) between perimenopausal and postmenopausal women, but not for TG ($F = 0.813$, $p = 0.371$), HDL ($F = 0.528$, $p = 0.470$), VLDL ($F = 0.601$, $p = 0.441$), TC/HDL ($F =$

Table 1. Demographic Data and Serum Lipid Levels of Perimenopausal and Postmenopausal Patients (mean ± SD)

| | Age (years) | BMI (kg/m ²) | TC (mg/dl) | TG (mg/dl) | HDL (mg/dl) | VLDL (mg/dl) | LDL (mg/dl) | TC/HDL | LDL/HDL |
|--------------------------------|----------------|-----------------------------|---------------|---------------|----------------|-----------------|----------------|---------|---------|
| Total (n = 69) | 48.4±4.1 | 23.8±2.9 | 201.7±32.0 | 115.2±63.8 | 53.8±12.0 | 22.8±12.7 | 125.0±27.3 | 3.9±1.0 | 2.3±0.7 |
| Perimenopausal status (n = 41) | 46.9±3.3 | 23.9±2.5 | 200.2±29.6 | 106.5±51.7 | 55.1±12.2 | 21.3±10.4 | 123.7±23.6 | 3.8±0.8 | 2.3±0.6 |
| Postmenopausal status (n = 28) | 50.5±4.2 | 23.8±3.4 | 203.9±35.7 | 138.6±115.6 | 52.0±11.8 | 29.3±30.5 | 122.6±34.8 | 4.1±1.2 | 2.5±0.9 |
| <i>p</i> value | | | 0.009* | 0.371 | 0.470 | 0.441 | 0.019* | 0.194 | 0.320 |

Abbreviations: BMI: body mass index; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; VLDL: very-low-density lipoprotein; LDL: low-density lipoprotein.

* Indicates a significant difference between perimenopausal and postmenopausal patients.

1.720, *p* = 0.194), or LDL/HDL (*F* = 1.004, *p* = 0.320).

Table 2 presents the depressive and anxious disorders, and serum lipid levels of 41 perimenopausal women. They were grouped into 3 categories: normal controls (n = 19), and those with anxiety disorders (n = 15) and depressive disorders (n = 7). Using ANCOVA adjusted for age, no significant differences were found in serum concentrations of TC (*F* = 0.513, *p* = 0.603), TG (*F* = 0.040, *p* = 0.961), HDL (*F* = 0.045, *p* = 0.956), VLDL (*F* = 0.036, *p* = 0.965), LDL (*F* = 1.084, *p* = 0.349), TC/HDL (*F* = 0.538, *p* = 0.589), or LDL/HDL (*F* = 0.805, *p* = 0.455) among the 3 groups. In addition, using ANCOVA adjusted for BMI, there were also no significant differences in serum concentrations of TC (*F* = 0.112, *p* = 0.894), TG (*F* = 0.565, *p* = 0.573), HDL (*F* = 0.210, *p* = 0.812), VLDL (*F* = 0.573, *p* = 0.569), LDL (*F* = 0.049, *p* = 0.952), TC/HDL (*F* = 0.186, *p* = 0.831), or LDL/HDL (*F* = 0.169, *p* = 0.845) among the 3 groups.

Table 3 presents data on the depressive and anxious disorders, and serum lipid levels of the 28 postmenopausal women. They were grouped into 3 cate-

gories: normal controls (n = 8), and those with anxiety disorders (n = 14) and depressive disorders (n = 6). Using ANCOVA adjusted for age, no significant differences were found in serum concentrations of TC (*F* = 0.160, *p* = 0.853), TG (*F* = 3.067, *p* = 0.067), HDL (*F* = 1.481, *p* = 0.264), VLDL (*F* = 2.836, *p* = 0.080), LDL (*F* = 0.057, *p* = 0.945), TC/HDL (*F* = 1.230, *p* = 0.312), or LDL/HDL (*F* = 0.066, *p* = 0.936) among the 3 groups. Furthermore, using ANCOVA adjusted for BMI, there were also no significant differences in serum concentrations of TC (*F* = 0.685, *p* = 0.515), TG (*F* = 0.106, *p* = 0.899), HDL (*F* = 1.427, *p* = 0.262), VLDL (*F* = 0.122, *p* = 0.885), LDL (*F* = 0.282, *p* = 0.757), TC/HDL (*F* = 0.072, *p* = 0.931), or LDL/HDL (*F* = 0.351, *p* = 0.708) among the 3 groups.

DISCUSSION

Our findings revealed that TC and LDL were higher in postmenopausal women than in perimenopausal women, which is consistent with other reports.^(28,29) These studies revealed that the lipid profile levels were higher in postmenopausal women.

Table 2. Serum Lipid Levels in Perimenopausal Women with Depressive or Anxious Disorders (mean ± SD)

| | Age (years) | BMI (kg/m ²) | TC (mg/dl) | TG (mg/dl) | HDL (mg/dl) | VLDL (mg/dl) | LDL (mg/dl) | TC/HDL | LDL/HDL |
|--|----------------|-----------------------------|---------------|---------------|----------------|-----------------|----------------|---------|---------|
| Total (n = 41) | 46.9±3.3 | 23.9±2.5 | 200.2±29.6 | 106.5±51.7 | 55.1±12.2 | 21.3±10.4 | 123.7±23.6 | 3.8±0.8 | 2.3±0.6 |
| Normal controls (n = 19) | 47.4±2.9 | 24.2±2.3 | 199.2±28.4 | 99.8±37.4 | 55.1±10.8 | 20.0±7.5 | 123.8±25.6 | 3.7±0.7 | 2.3±0.6 |
| Anxiety disorders (n = 15) | 46.5±3.1 | 23.2±2.5 | 199.9±26.0 | 111.8±48.2 | 54.6±12.9 | 22.4±9.6 | 122.9±22.4 | 3.8±0.8 | 2.4±0.7 |
| Panic disorder (n = 1) | 46.0 | 26.6 | 214.0 | 74.0 | 50.0 | 15.0 | 149.0 | 4.3 | 3.0 |
| Mixed anxiety-depressive disorder (n = 14) | 46.5±3.2 | 23.0±2.5 | 198.9±26.6 | 114.5±48.8 | 54.9±13.3 | 23.0±9.8 | 121.0±22.0 | 3.8±0.9 | 2.3±0.7 |
| Depressive disorders (n = 7) | 46.3±5.0 | 24.4±2.9 | 203.7±42.9 | 113.3±88.9 | 56.1±15.8 | 22.6±18.0 | 125.0±23.9 | 3.8±1.0 | 2.3±0.6 |
| Dysthymic disorder (n = 4) | 46.0±1.4 | 24.4±2.2 | 206.3±54.8 | 127.5±113.8 | 53.0±17.6 | 25.5±23.0 | 127.8±31.9 | 4.1±1.2 | 2.5±0.7 |
| Major depressive disorder (n = 3) | 46.7±8.4 | 24.4±4.2 | 200.3±31.6 | 94.3±58.0 | 60.3±15.5 | 18.7±11.6 | 121.3±12.5 | 3.4±0.6 | 2.1±0.4 |
| Significance | | | NS | NS | NS | NS | NS | NS | NS |

Abbreviations: BMI: body mass index; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; VLDL: very-low-density lipoprotein; LDL: low-density lipoprotein; NS: no significant difference among the normal controls and those with anxiety disorders and depressive disorders.

Table 3. Serum Lipid Levels in Postmenopausal Women with Depressive or Anxious Disorders (mean ± SD)

| | Age (years) | BMI (kg/m ²) | TC (mg/dl) | TG (mg/dl) | HDL (mg/dl) | VLDL (mg/dl) | LDL (mg/dl) | TC/HDL | LDL/HDL |
|--|----------------|-----------------------------|---------------|---------------|----------------|-----------------|----------------|-----------|-----------|
| Total (n = 28) | 50.5 ± 4.2 | 23.8 ± 3.4 | 203.9 ± 35.7 | 138.6 ± 115.6 | 52.0 ± 11.8 | 29.3 ± 30.5 | 122.6 ± 34.8 | 4.1 ± 1.2 | 2.5 ± 0.9 |
| Normal controls (n = 8) | 48.0 ± 3.6 | 22.4 ± 2.6 | 199.9 ± 30.6 | 136.8 ± 98.9 | 49.3 ± 12.5 | 27.1 ± 19.7 | 123.5 ± 30.0 | 4.3 ± 1.2 | 2.6 ± 0.8 |
| Anxiety disorders (n = 14) | 51.4 ± 3.9 | 23.9 ± 3.5 | 214.6 ± 37.9 | 135.5 ± 78.2 | 52.1 ± 11.2 | 25.8 ± 13.4 | 136.7 ± 31.5 | 4.3 ± 1.2 | 2.5 ± 0.9 |
| Panic disorder (n = 1) | 52.0 | 20.8 | 156.0 | 64.0 | 53.0 | 11.0 | 92.0 | 2.9 | 1.7 |
| Mixed anxiety-depressive disorder (n = 13) | 51.3 ± 4.1 | 24.1 ± 3.5 | 219.2 ± 35.3 | 141.0 ± 78.6 | 52.1 ± 11.6 | 26.9 ± 13.2 | 140.2 ± 29.9 | 4.4 ± 1.2 | 2.6 ± 0.9 |
| Depressive disorders (n = 6) | 51.8 ± 4.7 | 25.3 ± 4.0 | 184.0 ± 31.6 | 98.3 ± 38.1 | 55.3 ± 13.4 | 19.8 ± 7.4 | 108.8 ± 33.9 | 3.5 ± 1.1 | 2.1 ± 1.0 |
| Dysthymic disorder (n = 3) | 50.0 ± 4.4 | 23.2 ± 4.7 | 172.7 ± 15.6 | 75.0 ± 17.1 | 64.0 ± 6.2 | 15.3 ± 3.5 | 93.3 ± 15.3 | 2.7 ± 0.4 | 1.5 ± 0.4 |
| Major depressive disorder (n = 3) | 53.7 ± 5.1 | 27.4 ± 2.4 | 195.3 ± 43.2 | 121.7 ± 41.2 | 46.7 ± 13.6 | 24.3 ± 8.1 | 124.3 ± 43.8 | 4.3 ± 1.1 | 2.7 ± 1.0 |
| Significance | | | NS | NS | NS | NS | NS | NS | NS |

Abbreviations: BMI: body mass index; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; VLDL: very-low-density lipoprotein; LDL: low-density lipoprotein; NS: no significant difference among the normal controls and those with anxiety disorders and depressive disorders.

Their data also suggested that these differences in lipids and lipoproteins were due either directly or indirectly to an estrogen deficiency, which resulted from loss of ovarian function.

The relation between depressive symptoms and cholesterol has been reported to be age-dependent, and mainly present in older age groups (≥ 71 years),⁽³⁰⁾ although another study yielded contradictory results in the elderly.⁽¹⁰⁾ Other studies reported an association between low cholesterol and higher levels of depressive symptoms in younger (with a mean age of 21 ± 2.3 years),⁽⁴⁾ and middle-aged (30~65-year-old) women.⁽¹⁹⁾ However, in the present study, we observed no association of low cholesterol with depressive disorders in menopausal women.

In contrast to previous studies regarding the lifetime prevalence of mood disorders in women, our results suggest no correlation between lipid profiles and depressive or anxious states in menopausal women. Although our study was unable to address the direct relation between depression and cholesterol, some studies suggested that altered central metabolism related to low cholesterol levels could lead to depression.⁽⁷⁻⁹⁾ Engelberg suggested that a reduction in serum cholesterol may decrease brain-cell-membrane cholesterol, lower lipid micro-viscosity, and decrease exposure of protein serotonin receptors on the membrane surface, thus resulting in poorer uptake of serotonin from the blood and less serotonin entry into brain cells.⁽⁷⁾

Theoretically, perimenopausal women may be more susceptible to the effects of a changing milieu of reproductive hormones, which may lead to an increase in depression at the perimenopausal stage

more than in a postmenopausal status.⁽³¹⁾ Moreover, Horsten *et al.* investigated associations between cholesterol and other psychosocial factors (social support, vital exhaustion, and stressful life events), which are known to be related to depression in middle-aged women.⁽¹⁹⁾ Accordingly, the severity of anxiety and depressive symptoms may be influenced by environmental or reproductive hormonal factors, as well as by serum lipid levels.

This study had certain limitations. The numbers of peri- and postmenopausal subjects were too small, especial the group with depressive disorders, to draw any definitive conclusions regarding trends for prescribing practices for this population. In the future, cohort studies with a larger sample should be analyzed to control for many confounding variables.

In conclusion, our study revealed that TC and LDL were significantly higher in postmenopausal women compared to perimenopausal women. In addition, our results suggest that serum lipid profiles cannot serve as biological markers to distinguish depressive or anxious states in women during menopausal stages. In the future, larger samples are required to prove such results.

Acknowledgments

The authors wish to express their gratitude to Dr. J.Z. Shen for referring cases from the menopause clinic of the Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital.

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更年期婦女之憂鬱或焦慮疾患與血液中脂質的關聯

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- 背景：** 有數篇研究指出憂鬱或焦慮疾患與血中脂質的濃度有相關。在年輕、中年及產後的婦女，皆發現血中的膽固醇較低時，會有較高傾向的憂鬱症狀；但是很少有研究探討與更年期婦女的關係。故我們針對台灣更年期婦女設計一個研究，探討其憂鬱或焦慮疾患與血液中脂質的關聯。
- 方法：** 在這個為期兩年的橫段式研究中，有 69 位因停經症狀至婦產科門診求醫的更年期婦女被轉介至精神科做進一步的評估。其精神科診斷是依據精神疾病診斷及統計手冊第四版 (Diagnostic and Statistical Manual of Mental disorder, Fourth edition, DSM-IV) 之半結構式的臨床會談。在此同時收集病人血液檢體做為後續脂質濃度的分析。所有資料是經由 ANCOVA (analysis of co-variance) 來分析。
- 結果：** 在此研究中，發現停經後之婦女其血液中膽固醇 (TC) 和低密度脂蛋白 (LDL) 的濃度比停經前婦女高，但是在三酸甘油酯 (TG)、高密度脂蛋白 (HDL)、非常低密度脂蛋白 (VLDL)、膽固醇 / 高密度脂蛋白、以及低密度脂蛋白 / 高密度脂蛋白並沒有顯著的差異。此外，將停經前後的婦女依其精神症狀分為焦慮、憂鬱、及正常狀態等三組時，脂質濃度並無明顯差異。
- 結論：** 本研究顯示，在更年期的婦女，無法證實其血液中脂質之濃度可以當成區分焦慮或憂鬱疾患的生化指標。在未來，需要有更多的研究個案來加以驗證其關聯性。
(長庚醫誌 2006;29:325-30)

關鍵字： 憂鬱，焦慮，膽固醇，更年期，脂質。

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受文日期：民國94年8月1日；接受刊載：民國95年1月13日

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