

Comparison of psychiatric symptoms between patients with major depression with higher and lower levels of high-sensitivity C-reactive protein in the serum: a preliminary study

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To the Editor,

Inflammation plays an important role in the development of major depression (MD) and is a critical disease modification factor that promotes susceptibility to MD.^{1,2} Recent reports demonstrated that the altered levels of serum various cytokines and C-reactive protein (CRP) in MD patients may represent a homeostatic mechanism that enhances the inflammatory process during MD.^{3–5} Another report demonstrated that the variation of the patterns of cytokines is associated with the phenotype of major depression.⁶ One of the most common approaches to evaluate peripheral inflammation is to measure the serum levels of CRP. CRP plays a key role in the human inflammation process and can provide a proxy estimate for inflammatory activity.⁷ A systematic review and meta-analysis showed that CRP is a useful biomarker for investigating acute inflammatory processes in MD.⁸ Vegetative symptoms, but not cognitive symptoms of MD, were associated with higher CRP.^{9,10} The aim of the present study was to compare the psychiatric symptoms between MD patients with a higher level of high-sensitivity CRP (hsCRP) and a lower level of hsCRP in the serum. This study included 40 patients who met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for MD [male/female: 17/23, age: 56 (47–65; interquartile range) years]. We used the Montgomery Asberg Depression Rating Scale (MADRS) to evaluate depression severity. Blood samples were quickly separated using a centrifuge (2000 *g*, 15 min, 4°C)

and stored at –80°C until assay. We found that the serum hsCRP levels were not normally distributed in the histogram. We then classified 20 MD patients [male/female: 6/14, age: 55.5 (48–67) years] above the median (337 ng/m) as the higher hsCRP group and 20 MD patients [male/female: 10/10, age: 55 (46–62.5) years] below the median as the lower hsCRP group (Figure 1). The number of the depressive episodes were 1.5 (1–2) for the higher hsCRP group, and 2 (1–2) for the lower hsCRP group, respectively. The imipramine equivalence of dosage of antidepressants were 75 (37.5–225) mg/day for the higher hsCRP group, and 113 (89–150) mg/day for the lower hsCRP group, respectively. No differences were found between both groups regarding these factors. Mann-Whitney *U* test and Spearman's rank correlation were used for statistical analysis. Statistical significance was defined as $p < 0.05$. There was no significant difference in the total MADRS scores between the higher hsCRP group and the lower hsCRP group [12 (8–15) versus 13 (7.5–19), $p = 0.29$]. Regarding the MADRS score for each item, only reduced appetite showed a significant difference [0 (0–2) versus 2 (1–3), $p = 0.024$] (Table 1). The body mass index did not differ between the groups [25 (22–28) versus 23 (19–26) kg/m²]. A recent report demonstrated that poor appetite and low food intake are associated with inflammation in older hospitalized patients.¹¹ In addition, inflammation is associated with hedonic inferences about food stimuli using a functional magnetic resonance imaging (fMRI) scan.¹² The results of our study were not in agreement with

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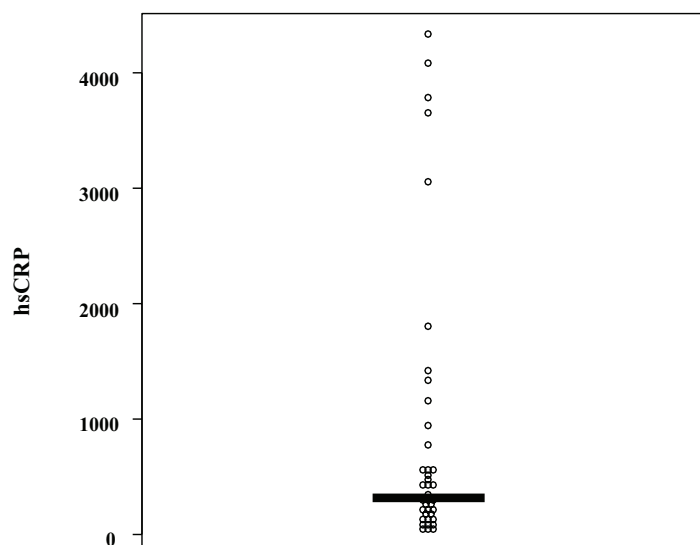


Figure 1. Distribution of serum levels of hsCRP in MD patients.

Table 1. Scores for each criterion of the MADRS between both groups.

	Higher hsCRP group (<i>n</i> = 20)	Lower hsCRP group (<i>n</i> = 20)	<i>p</i> value
Apparent sadness	2 [1–2]	2 [2–2]	0.15
Reported sadness	2 [1–2.5]	2 [1–3]	0.47
Inner tension	2 [1–2]	1 [1–2]	0.87
Reduced sleep	2 [2–4]	2 [2–4]	1.0
Reduced appetite	0 [0–2]	2 [1–3]	0.024
Concentration difficulty	2 [2–2]	2 [2–3]	0.49
Lassitude	1 [1–2]	2 [1–2]	0.35
Inability to feel	2 [1–2.5]	2 [1–4]	0.17
Pessimistic thoughts	1 [1–2]	2 [1–3]	0.26
Suicidal thoughts	1 [1–2]	1 [1–3]	0.92

hsCRP, high-sensitivity C-reactive protein; MADRS, Montgomery Asberg Depression Rating Scale.
Data are expressed as median [interquartile range].
Statistically significant differences ($p < 0.05$) are in bold.

the previous findings that higher CRP levels were associated with vegetative symptoms and reduced food intake. The discrepancy between the results of the present study and those of recent studies^{9,10,12} remains unknown. Many factors may be involved in the regulation of appetite in MD. The limitations of this study include its small sample size, mild to moderate severity of MD, and the influence of antidepressants in the present study.

There were no differences in the dosage of antidepressants to imipramine equivalence between the groups as we mentioned. The most serious problem in the present study is a lack of control group. In conclusion, reduced appetite might be associated with lower hsCRP levels in MD patients. Comparing serum hsCRP levels with those with healthy subjects might lead to a rational interpretation of this preliminary result.

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Author contributions

NO and TH were involved in the clinical investigations. NO and RY drafted the manuscript. NO performed a statistical analysis of the data. AI, TH, and RY conducted the literature review and corrections. All authors have read and approved the final manuscript.

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Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics statement

We obtained a written informed consent from all the participants. This study was approved by the Ethics Committee of the University of Occupational and Environmental Health Kitakyushu, Japan (approval number: UOHECRB21-057) and followed the tenets of Helsinki Declaration.

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Availability of data and materials

The data sets used and/or analyzed during the current case report are available from the corresponding author upon reasonable request.

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