

Oxidative Balance Scores in Adults with Suicidal Ideation: A Nationwide Korean Survey

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ABSTRACT

This cross-sectional study investigated the relationship between oxidative balance (OB) scores and suicidal ideation among the Korean adults. Data from 17,753 adults with information on suicidal ideation and OB scores were analysed using four years of the nationwide survey. A stepwise multivariate logistic regression model was used to catch the factors associated with suicidal ideation, including depressive mood and OB scores. Approximately 5% of the participants had suicidal ideation. Low OB scores were significantly and independently associated with suicidal ideation, and this association was not influenced by depressive mood. In conclusion, oxidative imbalance was related to suicidal ideation, independent of depressive mood.

Key Words: Depression, Oxidative stress, Population surveillance, Suicidal ideation.

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Suicide is a critical mental health problem and suicidal behaviours have various risk factors, including demographics, internalising or externalising psychopathology, and psychosocial factors; biomarkers have received recent attention as a potential risk factor as well. In particular, research has examined oxidative markers and whether they are associated with affective disorders¹ based on high utilisation of oxygen and poor antioxidant defence in the brain. The role of oxidative stress in depression and the strong association between suicidal behaviours and depressive episodes have been unequivocally established.² However, the role of oxidative stress in suicidal behaviour— independent of depressive mood—has not yet been clarified.

Several oxidative biochemical markers are associated with suicidal behaviour. Suicide attempters have shown decreased plasma levels of brain-derived neurotrophic factor, omega-3 polyunsaturated fatty acids, vitamin D, and carotenoids, all indicating lowered antioxidant defences. A recent Iranian study reported both higher levels of oxidative stress and lower levels of antioxidants in suicide attempters.³ Oxidative stress is generated when free radical production is over the antioxidant capacity. An oxidative balance (OB) scoring system was developed to semi-quantitatively measure oxidative stress, and a few studies have examined the association between these scores and various health outcomes.⁴

In this national study, the authors investigated the independent association of suicidal ideation with OB scores among the Korean adults, highlighting how to detect high-risk subjects and facilitating the investigation of the pathogenesis of suicidal behaviour.

The authors utilised data from the 2013, 2015, 2017, and 2019 Korean National Health and Nutrition Examination Surveys (KNHANES), which questioned adults aged ≥ 19 years about suicidal ideation. It included 17,753 participants with information on OB scores and suicidal ideation in the final analysis.

The main outcome of this study was suicidal ideation, which was assessed *via* the self-reported yes/no question: "Have you thought about committing suicide within the last 12 months?" OB scores were a *priori* determined for 10 components related to oxidative stress, including five pro-oxidant factors and five antioxidant factors.⁴ The maximum OB score was 30 points—higher scores indicated antioxidant predominance.

Demographic features (age, gender, marital status, economic status, and attained education level), comorbid conditions (hypertension, type 2 diabetes, and major critical diseases [myocardial infarction, stroke, and cancer]), and depressive mood were also analysed as covariates. Mean monthly household income was used as an indicator of economic level. Unmarried subjects included those who reported being divorced, separated for any reason, or single. Education level was grouped as middle school or lower or high school or beyond. Comorbidities were based on the diagnoses by physicians. For the depressive mood, responses to the yes/no questionnaire item were used: Have you experienced sadness or despair continuously for more than two weeks during the past year? Patients with current treatment for depressive disorder were considered as having depressive mood.

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Table I: Factors related to suicidal ideation, including OB score.

Variables	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (per 1 year)	1.02 (1.01-1.02)	<0.001		
Female	1.25 (1.09-1.43)	0.001		
Low income ^a	2.80 (2.43-3.22)	<0.001	1.68 (1.42-1.98)	<0.001
Unmarried ^b	1.89 (1.65-2.17)	<0.001	1.33 (1.14-1.56)	<0.001
Low education ^c	2.47 (2.15-2.83)	<0.001	1.43 (1.22-1.69)	<0.001
Hypertension	1.58 (1.36-1.83)	<0.001		
Type 2 diabetes	2.04 (1.68-2.47)	<0.001	1.37 (1.09-1.71)	0.007
Major critical disease ^d	1.70 (1.38-2.09)	<0.001		
Depressive mood	18.65 (16.09-21.62)	<0.001	15.87 (13.61-18.52)	<0.001
OB score (per 1-point)	0.93 (0.91-0.95)	<0.001	0.94 (0.92-0.96)	<0.001

OB, Oxidative balance; OR, Odds ratio; CI, Confidence interval. ^aAverage household income or lower; ^bincludes divorced, separated, and single; ^cmiddle school education or less; ^dincludes myocardial infarction, stroke, and cancer.

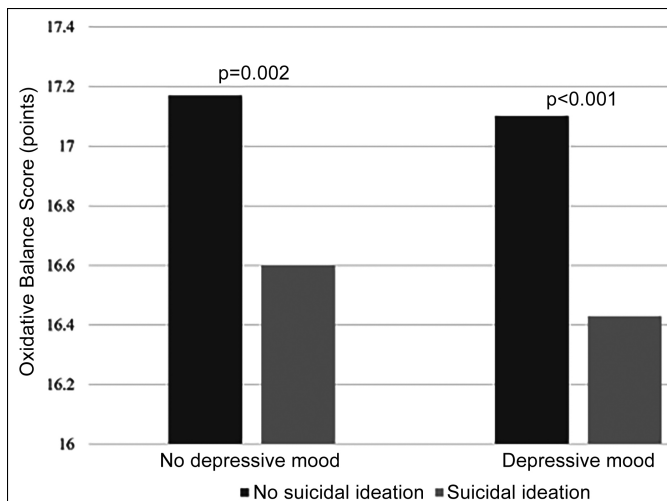


Figure 1: Oxidative balance score by suicidal ideation in depressed and non-depressed subjects. Oxidative balance score was estimated using multivariate regression analysis adjusted for age, gender, income, marital status, attained education, and comorbidities (hypertension, type 2 diabetes, and major critical diseases, such as myocardial infarction, stroke, and cancer).

A stepwise multivariate logistic regression model adjusted for potential confounders was used to find the factors related to suicidal ideation. OB scores were estimated from the multivariate regression analysis according to depressive mood and suicidal ideation. The analysis was conducted using Stata/MP version 17.0 (Stata Corp., College Station, TX, USA), and p-values less than 0.05 were considered significant.

Median age (interquartile range) of total population was 50 (37-63) years. Proportion of married people and people with high school graduate or beyond was 70.7% and 71.6%, respectively. Approximately 5% of participants had suicidal ideation. Subjects with suicidal ideation were older, female, poorer, unmarried, and more depressive and had low educational attainment, more comorbidities, and lower OB scores (data not shown).

Stepwise multivariate logistic analysis revealed that low income, unmarried status, low educational attainment, type 2 diabetes, depressive mood, and low OB scores were associated with suicidal ideation (Table I).

Sensitivity analysis revealed that depressive mood did not influence the association between OB scores and suicidal ideation (Figure 1).

To the best of the authors' knowledge, this is the largest study of the association between oxidative status and suicidal behaviours to date. Most prior studies were conducted in specific settings (e.g., among patients with major depressive disorders or psychiatric disorders),⁵ and research with healthy controls—even with small sample sizes—has been rare. Additionally, nearly all related studies investigated specific markers, whereas the authors used OB scores, which offer a composite index that may be useful in practice. Finally, suicidal behaviours cover a broad spectrum, including completed suicide, suicide attempts, and suicidal ideation. The effects of oxidative markers may be the lowest for individuals with suicidal ideation alone.⁵ Moreover, the authors assessed suicidal ideation during the past year instead of a more recent period (e.g., within three months). Therefore, the study design had lower feasibility for achieving statistical significance.

Depression substantially contributes to suicidal behaviour, but it is not the only contributing factor. In this study, it is noteworthy that the relationship between oxidative imbalance and suicidal ideation was independent of depressive mood. Some pathways may explain this independent association,⁶ although they require further exploration. First, oxidative imbalance may cause neuroprogression linked to suicide through other inflammatory pathways. Next, oxidative stress may facilitate the production of tryptophan catabolites (e.g., kynurenine), which causes decreased levels of serotonin. A 5-HT_{1A} receptor binding of serotonin has been found to be greater in suicides, independent of depression.

This study has several limitations. First, the cross-sectional design precludes inferences of temporal relationships. Second, the OB scoring system has basic limitations: It does not reflect endogenous factors, the dietary factors are exposed to recall bias, and the threshold effects of antioxidants were not concerned. Third, the generalisability of the present study's results is limited as Western cultures is

marked by extremely different dietary habits, lower suicidal rates, and better strategies for dealing with distress. Future cohort or case-control studies, particularly in other countries, are necessary to confirm or refute these findings.

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ETHICAL APPROVAL:

All participants provided written informed consent, and researchers followed the guidelines set forth in the Declaration of Helsinki. The Institutional Review Board (IRB) of Gachon University Gil Medical Centre (IRB No: GFIRB2022-099) approved the study protocol.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

JHL, KDK: Interpretation and manuscript preparation.

ICH: Conceptualisation, methodology, manuscript review, and editing.

HYA: Formal analysis and interpretation.

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