

Relationship Between Ketone Levels, Anxiety, and Stress in Older Adults



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Introduction

- The global prevalence of stress and anxiety in older adults is 16.5% and 13.9%, respectively; yet these common mental health concerns are often overlooked in older adults.¹
- In recent years, studies have found a link between diet and mental health, with ketogenic diets, in particular, associated with psychological well-being.^{2,3} Ketone bodies have been linked to an increase in mitochondrial density⁴ and a decrease in mitochondrial abnormalities that are associated with symptoms of depression and anxiety.⁵
- In multiple animal models, researchers have found that ketone supplementation is associated with lower anxiety⁶ and stress-induced impairments⁷. Case studies in humans show a similar trend for improvements in anxiety.^{8,9} The few human studies that focused on this topic have inconclusive evidence regarding the effect of ketone levels on anxiety and stress.¹⁰
- As such, it is critical to investigate the link between ketone bodies, anxiety, and stress in this understudied population.

Hypothesis

- Higher ketone levels will be associated with lower anxiety and stress in older adults.

Methods

Participants

- 10-week data were collected from a dietary intervention study; data from 32 participants who were assigned to the Mediterranean ketogenic diet arm were analyzed in this paper.
- The sample was composed of community-dwelling older adults between the ages of 57 and 85, with and without mild cognitive impairment.

Measures

- Covariates: age, sex (coded as 0 = Female and 1 = Male), and education level (coded as 0 = Did not complete middle school, 1 = Did not complete high school, 2 = High school diploma, 3 = Some college, 4 = Associate's degree, 5 = Trade school certificate, 6 = Bachelor's degree, 7 = Master's degree, 8 = Doctoral degree).
- Anxiety** was measured at a 10-week follow-up appointment using the total score from the Geriatric Anxiety Scale.¹¹
- Stress** was measured at a 10-week follow-up appointment using the total score from the Perceived Stress Scale (PSS).¹²
- Total **ketone levels** from 10-week data were dichotomized into two groups based on whether they were above or below the ketone trace level (0 = No, 1 = Yes). Ketone levels were measured using daily at-home urinalysis test strips. Participants logged daily levels and reported them using weekly surveys.

Analysis

- Data was analyzed using hierarchical linear regression in SPSS.

Results

Sample Characteristics

- Participants were predominantly female, with a bachelor's level of education on average. Participants tended to report relatively low levels of anxiety and stress.
- Approximately 62% of the sample achieved measurable levels of ketones during the intervention.

Table 1

Descriptive Statistics for Participants			
	Frequencies	M	SD
Gender			
Female	26	-	-
Male	6	-	-
Age	-	70.64	4.62
Education Level			
Did not complete high school	1	-	-
High school diploma	3	-	-
Some college	1	-	-
Associate degree	5	-	-
Bachelor's degree	9	-	-
Master's degree	10	-	-
Doctoral degree	3	-	-
Geriatric Anxiety Scale total scores	-	2.77	2.99
Perceived Stress Scale total scores	-	8.52	4.84
ketone Levels			
Above trace level	18	-	-
Below trace level	11	-	-

Ketone Level and Anxiety

- There was a statistical trend for higher ketone levels to be associated with higher anxiety ($B = .33, p = .072$).

Table 2

Correlations Between Ketone Levels, Demographic Information, and Dependent Variable

Variable	Unstandardized	Coefficients	Standardized	t	Sig.
	B	Std. Error	Coefficients		
			B		
Age	-0.22	0.12	-0.33	-1.87	0.07
Sex	-1.50	1.25	-0.20	-1.20	0.24
Education	0.21	0.27	0.13	0.77	0.48
Ketone levels	2.07	1.10	0.33	1.88	0.07

*Dependent variable: Total Geriatric Anxiety Scale Score

Ketone Level and Stress

- Accounting for covariates, ketone levels were not significantly associated with stress ($B = .23, p = .183$).

Table 3

Correlations Between Ketone Levels, Demographic Information, and Dependent Variable

Variable	Unstandardized	Coefficients	Standardized	t	Sig.
	B	Std. Error	Coefficients		
			B		
Age	-0.35	0.18	-0.33	-1.92	0.07
Sex	-3.66	2.00	-0.30	-1.82	0.08
Education	-0.43	0.43	-0.17	-1.00	0.33
Ketone levels	2.32	1.69	0.23	1.37	0.18

*Dependent variable: Total Perceived Stress Scale Score

Conclusions

- Contrary to expectations and prior research,⁹ the results did not support the hypothesis, as high ketone levels were not associated with low stress and anxiety in older adults. In fact, there was a trend for participants to report higher anxiety among those who achieved ketosis.
- The differences between our findings and past literature may be more likely to be attributed to behavioral factors. In a previous clinical study, participants who self-reported as having higher anxiety levels at baseline (non-clinical) had higher adherence to the ketogenic diet, leading to higher ketone levels.¹³
- A possible explanation for these findings could be found in the concept of eustress or "good" stress. Previous literature supports the idea that eustress could facilitate advantageous adaptive behavioral outcomes, which in turn increase positive health behaviors such as diet adherence.¹⁴
- Due to the use of a correlational design in this paper, we are unable to establish causality. As such, it could be that anxiety affects ketone levels, or that ketone levels could affect anxiety.
- A larger sample may be needed to detect a significant relationship between the variables, as small samples have low statistical power, thus a relationship could only be detected if the effect is large.

Future directions

- Given that there is a sizeable number of studies on animal models that explore the therapeutic effects of ketone supplements, future clinical studies should aim to explore how exogenous ketogenic supplements can affect anxiety and stress in older adults.
- Future research could also focus on how age can affect the anti-stress potential of elevated ketone levels through a longitudinal study.

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