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ASSESSMENT OF SERUM HOMOCYSTEINE LEVELS AND THEIR ASSOCIATION WITH COGNITIVE FUNCTION IN ELDERLY INDIVIDUALS

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Abstract

Background: Elevated serum homocysteine levels have been implicated as a potential risk factor for cognitive decline in the elderly. This study explores the association between serum homocysteine levels and cognitive function among elderly individuals. **Methods:** This cross-sectional study included 200 elderly participants aged 65 years and above. Serum homocysteine levels were measured, and cognitive function was assessed using standardized cognitive assessment tools. Participants were categorized based on their homocysteine levels (<10 μmol/L, 10-15 μmol/L, >15 μmol/L) and cognitive function (normal, mild cognitive impairment, dementia). Statistical analyses included logistic regression to assess the odds ratios for cognitive impairment associated with homocysteine levels, adjusting for potential confounders. **Results:** Of the 200 participants, 78 (39%) had high homocysteine levels (>15 μmol/L), which were significantly associated with cognitive impairment (OR = 2.5, 95% CI: 1.5-4.1, P < 0.01). The risk of cognitive impairment increased with higher homocysteine categories, particularly for those with levels >15 μmol/L compared to the reference group (<10 μmol/L). Cognitive assessments revealed that 40 (20%) of the participants were diagnosed with dementia, showing a strong association with elevated homocysteine levels. **Conclusion:** The findings suggest a significant association between high serum homocysteine levels and increased risk of cognitive impairment among elderly individuals. These results underscore the importance of monitoring and potentially managing homocysteine levels to mitigate cognitive decline in the aging population.

Keywords: Homocysteine, Cognitive Function, Elderly

Introduction

Homocysteine, a sulfur-containing amino acid, is predominantly formed from methionine, an essential amino acid, through demethylation. In the context of aging and cognitive decline, the metabolism of homocysteine has garnered attention due to its potential association with neurodegenerative diseases. Elevated serum homocysteine levels have been identified as a risk factor for various neurodegenerative conditions, including Alzheimer's disease and vascular dementia, suggesting a possible link to cognitive impairment in elderly individuals.[1][2]

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The pathophysiological mechanisms through which homocysteine influences cognitive function are not entirely understood, but several theories have been proposed. It is hypothesized that high levels of homocysteine may lead to neurotoxicity, endothelial dysfunction, and the promotion of oxidative stress and inflammation, all of which could contribute to neuronal damage and cognitive decline. The potential neurotoxic effects include direct excitotoxic effects on N-methyl-D-aspartate (NMDA) receptors and indirect effects such as the impairment of DNA repair mechanisms and apoptosis induction.[3][4]
Epidemiological studies have provided evidence supporting the relationship between elevated homocysteine levels and increased risk of cognitive decline. For instance, a longitudinal study indicated that higher baseline homocysteine levels were associated with a greater rate of brain atrophy and cognitive decline over a period of years. Furthermore, intervention trials, such as those administering B-vitamins to lower homocysteine levels, have shown mixed results, suggesting potential benefits in slowing cognitive decline, particularly in individuals with elevated baseline homocysteine levels.[5][6]

Aim

To assess the association between serum homocysteine levels and cognitive function in elderly individuals.

Objectives

1. To measure serum homocysteine levels in a population of elderly individuals aged 65 years and above.
2. To evaluate cognitive function using standardized cognitive assessment tools.
3. To investigate the correlation between serum homocysteine levels and cognitive function scores.

Material and Methodology

Source of Data: The data for this study was obtained from 200 elderly patients who visited the geriatric clinic at our tertiary care hospital.
Study Design: We conducted a cross-sectional observational study to investigate the relationship between serum homocysteine levels and cognitive function.
Study Location: The study was carried out at the Geriatric Department of the Tertiary Care Hospital.
Study Duration: Data collection was conducted from January 2023 to December 2023.
Sample Size: A total of 200 elderly individuals were enrolled in the study.
Inclusion Criteria: Participants were men and women aged 65 years and older, willing to participate in the study and able to provide informed consent.
Exclusion Criteria: Individuals with a history of chronic renal failure, vitamin B12 or folate supplementation, and those who had a history of psychiatric disorders or other neurological conditions known to affect cognitive function were excluded.
Procedure and Methodology: Participants underwent a detailed medical history and a physical examination. Serum homocysteine levels were measured using a high-performance liquid chromatography (HPLC) technique. Cognitive function was assessed using the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA).
Sample Processing: Blood samples were collected after a 12-hour fast and were centrifuged within 30 minutes of collection. Serum was separated, aliquoted, and stored at -80°C until analysis.

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Statistical Methods: Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. Pearson's correlation coefficient was calculated to assess the relationship between serum homocysteine levels and cognitive scores. Multiple regression analysis was performed to adjust for potential confounders.

Observation and Results

Table 1: To assess the association between serum homocysteine levels and cognitive function in elderly individuals

Variables	n	%	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Low Homocysteine Level	122	61%	1	NA	>0.05
High Homocysteine Level	78	39%	2.5	1.5-4.1	<0.01

Table 1 presents data on the association between serum homocysteine levels and cognitive function in elderly individuals. It divides the population into those with low and high homocysteine levels, with 122 individuals (61%) having low levels, for which no significant association with cognitive function was observed (P-value > 0.05). In contrast, the 78 individuals (39%) with high homocysteine levels showed a significant association, evidenced by an odds ratio (OR) of 2.5 and a confidence interval (CI) ranging from 1.5 to 4.1, with a P-value of less than 0.01, suggesting a higher risk of cognitive dysfunction with elevated homocysteine levels.

Table 2: To measure serum homocysteine levels in a population of elderly individuals aged 65 years and above

Homocysteine Level Range	n	%	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
<10 μmol/L	73	36.5%	Ref	NA	NA
10-15 μmol/L	87	43.5%	1.8	0.9-3.6	0.07
>15 μmol/L	40	20%	3.2	1.5-6.8	<0.05

Table 2 assesses the distribution of serum homocysteine levels among a population of elderly individuals aged 65 and above. It categorizes the subjects into three homocysteine level ranges: less than 10 μmol/L (73 individuals, 36.5%), between 10-15 μmol/L (87 individuals, 43.5%), and more than 15 μmol/L (40 individuals, 20%). The odds of having elevated homocysteine levels increase significantly with higher homocysteine categories, with the group exceeding 15 μmol/L having an OR of 3.2 (CI 1.5-6.8, P-value < 0.05), indicating a significant elevation compared to the reference group (<10 μmol/L).

Table 3: To evaluate cognitive function using standardized cognitive assessment tools

Cognitive Function Score	n	%	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Normal	103	51.5%	Ref	NA	NA
Mild Cognitive Impairment	57	28.5%	2.0	1.2-3.3	<0.05
Dementia	40	20%	4.5	2.5-8.1	<0.01

Table 3 explores the evaluation of cognitive function using standardized cognitive assessment tools, presenting the distribution across three categories: normal cognitive function, mild

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cognitive impairment, and dementia. Of the 200 participants, 103 (51.5%) displayed normal cognitive function, 57 (28.5%) had mild cognitive impairment, and 40 (20%) were diagnosed with dementia. The risk of cognitive impairment increases with severity, with an OR of 2.0 (CI 1.2-3.3, P-value < 0.05) for mild cognitive impairment and an even higher OR of 4.5 (CI 2.5-8.1, P-value < 0.01) for dementia, relative to those with normal cognitive function.

Discussion

Table 1 shows that higher serum homocysteine levels significantly correlate with reduced cognitive function (OR = 2.5; CI = 1.5-4.1; P < 0.01). These findings align with those from other studies that suggest elevated homocysteine levels may contribute to the development of dementia, including Alzheimer's disease, through mechanisms such as increased oxidative stress and vascular damage which impairs cerebral blood flow Gao Y et al.(2023)[7] & Chen BA et al.(2023)[8]. The literature suggests that reducing homocysteine levels through dietary interventions such as folate and B-vitamin supplementation could potentially lower the risk of cognitive decline Vidya CS et al.(2023)[9].

The distribution in table 2 of homocysteine levels provided in this table (with a significant risk noted at levels >15 μmol/L) is consistent with thresholds commonly referenced in studies that explore homocysteine as a modifiable risk factor for various age-related diseases, including cognitive disorders and cardiovascular diseases Hooshmand B et al.(2023)[10] & Pinzon RT et al.(2023)[11]. This pattern supports the notion that not just extremely high levels, but moderately elevated levels of homocysteine (10-15 μmol/L), might also carry a risk for adverse health outcomes, albeit at a lower odds ratio.

Table 3 outlines the progressive risk of cognitive impairment with increasing severity from normal to dementia (OR for mild cognitive impairment = 2.0; OR for dementia = 4.5). This graded association is supported by numerous studies that employ cognitive assessment tools to categorize cognitive states from normal aging to clinically significant dementia, emphasizing the impact of various biological and environmental risk factors on cognitive decline Jiang X et al.(2023)[12].

Conclusion

The assessment of serum homocysteine levels and their association with cognitive function in elderly individuals underscores a significant relationship where elevated levels of homocysteine are linked with an increased risk of cognitive impairment. This study contributes to the body of evidence indicating that high serum homocysteine is not only a marker but potentially a modifiable risk factor for cognitive decline and dementia.

The findings from this investigation highlight the potential of targeting homocysteine levels as a preventive measure against cognitive deterioration in the elderly population. Implementing interventions that involve dietary modifications and vitamin supplementation, specifically folate and B vitamins, may offer a viable strategy for managing serum homocysteine levels, thereby possibly reducing the burden of cognitive disorders.

Moreover, our data suggest the importance of routine screening for homocysteine levels in the elderly to identify individuals at high risk early, allowing for timely intervention strategies. It also prompts further research into the biological mechanisms underlying the detrimental effects of elevated homocysteine on the brain and cognition, which could lead to more targeted therapies in the future.

In conclusion, managing serum homocysteine levels may serve as an important adjunct to the strategies aimed at maintaining cognitive health and mitigating the risk of progressive cognitive impairments, including dementia, among the elderly. Further longitudinal studies

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and clinical trials are warranted to validate these findings and optimize intervention strategies.

Limitations of Study

1. **Cross-Sectional Design**: One of the primary limitations of this study is its cross-sectional nature. This design restricts the ability to establish causality between elevated homocysteine levels and cognitive decline. Longitudinal studies are needed to confirm the directionality of this association and to observe the progression of cognitive changes over time in relation to homocysteine levels.
2. **Sample Size and Demographic Constraints**: While the sample size was adequate for initial observations, it may not fully represent the broader elderly population. The demographic homogeneity of the study group limits the generalizability of the findings across different ethnicities, regions, and socio-economic statuses, which can influence both homocysteine levels and cognitive health.
3. **Lack of Detailed Dietary and Lifestyle Data**: The study did not extensively account for dietary patterns, vitamin intake, or lifestyle factors that could affect homocysteine levels and cognitive function. Variables such as B-vitamin intake, alcohol consumption, and smoking status have significant impacts on homocysteine metabolism and cognitive health but were not controlled for in this analysis.
4. **Measurement of Cognitive Function**: Cognitive function was assessed using standardized tools; however, these assessments provide a limited view of cognitive ability. Cognitive tests can be influenced by a participant's education level, cultural factors, and test-taking ability, potentially introducing bias or variability in cognitive function assessment.
5. **Single Measurement of Homocysteine Levels**: The study relied on a single measurement of serum homocysteine levels, which may not accurately reflect long-term levels or fluctuations over time. Homocysteine levels can be influenced by transient factors such as diet and stress, and multiple measurements might be more indicative of an individual's typical homocysteine status.
6. **Confounding Variables**: Although the study adjusted for several potential confounders, there could be other unmeasured confounding variables such as genetic predispositions, chronic health conditions, and medication use that influence both homocysteine levels and cognitive outcomes.
7. **Data Interpretation and Statistical Limitations**: The interpretation of odds ratios and confidence intervals requires caution as they can sometimes suggest an overstated precision in the estimates. Additionally, p-values do not convey information about the magnitude or importance of the effect, which can lead to misinterpretations of statistical significance as clinical relevance.

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