IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 8 Ver. II (Aug. 2015), PP 26-29
www.iosrjournals.org

Correlation between Haemoglobin Levels and Verbal Memory among an Older Adult Population in Chennai

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Abstract:
Introduction: *Older adults constitute a considerable and growing part of the Indian population. Normal levels of haemoglobin are associated with better survival. Anaemia is common among the elderly and it becomes more so with advancing decades.*
Aim of the study: *To analyze the immediate and delayed verbal memory status among older adult population in Chennai aged between 50 – 65 years and its relationship with differing levels of Haemoglobin.*
Material and methods: *The study was conducted among a total of 304 older adult subjects inclusive of both genders and aged between 50 to 65 years. After screening with inclusion and exclusion criteria the haemoglobin estimation was done and cognition was assessed using standard questionnaires. Comparison of the varying levels of haemoglobin with the measures of verbal memory was done.*
Results and discussion: *Immediate and delayed Verbal memory scores in the normal haemoglobin group were higher than the low haemoglobin group and the results were statistically significant. (p=0.000). We were able to observe that low haemoglobin levels are related to decrements in specific domains of verbal memory. Low haemoglobin may be a marker for the presence of conditions such as ischemia, hypoxia, altered erythropoietin levels and oxidative stress.*
Conclusion: *Low haemoglobin levels were associated with decreased cognitive functions in the domains of immediate and delayed verbal memory.*
Key words: *haemoglobin levels, verbal memory, older adults*

I. Introduction

Older adults constitute a considerable and growing part of the Indian population. Scientific inputs assisting to delay the physiological process of ageing has been an integral goal of modern physiology research as greater independence in life leads to a better quality of life particularly true among the elderly.

Normal levels of haemoglobin are associated with better survival. An increase in haemoglobin levels would be accompanied by significant improvement in cognitive performance; whereas, low haemoglobin level are a marker for the presence of Hypoxia and oxidative stress and is a potential contributing factor for cognitive impairment among older adults. As the prevalence of anaemia and consequently its impact on health and health care expenditure is expected to rise, a better understanding of the Neurophysiology related to anaemia in the elderly will lead to improved targeted treatment strategies.

Anaemia is common among the elderly and it becomes more so with advancing decades, this stems from a progressive decrease in the haemoglobin levels due to various reasons including progressive decline in glomerular filtration rate (GFR) and the associated reduction in production of erythropoietin, reduced concentration of testosterone and dehydroepiandrotestosterone (DHEA), growth hormone, insulin, thyroxine, and increased levels of concentration of corticosteroids. Moreover there will be a reduction in the ability to counter hemopoietic stress due to a progressive reduction in marrow cellularity as well.

Ageing related decrease in gastric secretion of hydrochloric acid, pepsin and gastric motility, reduced circulation in splanchnic areas and in the surface available for absorption of nutrients leads to vitamin B12 deficiency which leads to anaemia and various neurologic disorders including dementia, and posterior column lesions. Ageing leads to memory decline and cognitive slowing, even to a level that interferes with daily routine activities. Cognitive neuroscience studies relates the cognitive changes to the changes in the neural substrates, including structural and functional changes in prefrontal cortex, medial temporal lobe regions and white matter tracts thus placing a larger thrust on neuro imaging techniques (Trey Hidden; 2004).

II. Aim Of The Study

To analyse the immediate and delayed verbal memory status among an older adult population in Chennai aged between 50 – 65 years and its relationship with differing levels of Haemoglobin.

III. Material And Methods

After obtaining Institutional Ethical Committee clearance, the cross sectional study was conducted in Sri Ramachandra Hospital, Porur, Chennai among a total of 304 subjects inclusive of both genders and aged between 50 to 65 years. Subjects with neurological disorders, Alzheimer's disease and dementia diseases were excluded by a screening test using Mini Mental State Examination. Subjects with hematological diseases were also excluded. Informed written consent was taken prior to the study from all subjects, and then a structured questionnaire was administered. During the study, haemoglobin status was assessed by a complete blood count; assessment of cognitive function was done by a battery of cognitive function tests, the haemoglobin levels were correlated with the results obtained from the cognitive tests. Data entry was done and the data analysis was performed with SPSS software 15.0.

Elders with poorer health state, less education and less control of their environment, would consider themselves to have more memory problems; hence we have designed this study to exclude the subjects with ill health by doing a screening test using the standardized mini mental state assessment questionnaire. Subjects with satisfactory results alone were accepted to participate in the study. Chronic kidney disease and pulmonary disease are associated with decreased production of hypoxia inducible factor, may lead to reduced production of erythropoietin levels leading to an increased risk for neuronal degeneration in certain cognitive pathways. Hence subjects with reduced renal, pulmonary and cardiac and other circulatory functions were also excluded.

Blood samples were collected by utilizing standard procedures using sterile technique, blood specimen was collected in 3 ml sterile violet colored vacuum tubes with ethylenediaminetetraacetic acid (EDTA) by the phlebotomists and nurses skilled in venipuncture. Complete blood count analysis was done using a Sysmax X T 2000 I fully automated processor, and results were obtained in 45 seconds. According to this method the normal range of haemoglobin for males is 13 -17 gm/dl and for females it is 12 – 15 gm/dl.

Verbal memory is a subtest from the Wechsler memory scale – III. In this task there are 2 stories. Each story will be presented before the subject orally and the subject will be asked to reproduce the story from the memory as much as possible. After the completion of first story another story will be presented and the same procedure will be repeated as the first one for taking the measures of immediate verbal memory. The subjects were asked for demographic information including date of birth, highest number of years of education completed, gender and details regarding personal and family history. Hhaemoglobin estimation was done and cognition was assessed using standard questionnaires. We compared the varying levels of haemoglobin with the measures of verbal memory.

IV. Results And Discussion

Table 1.1 - Age of the participants

	N	Minimum	Maximum	Mean	Std. Deviation
Age	304	50	65	58.45	4.270

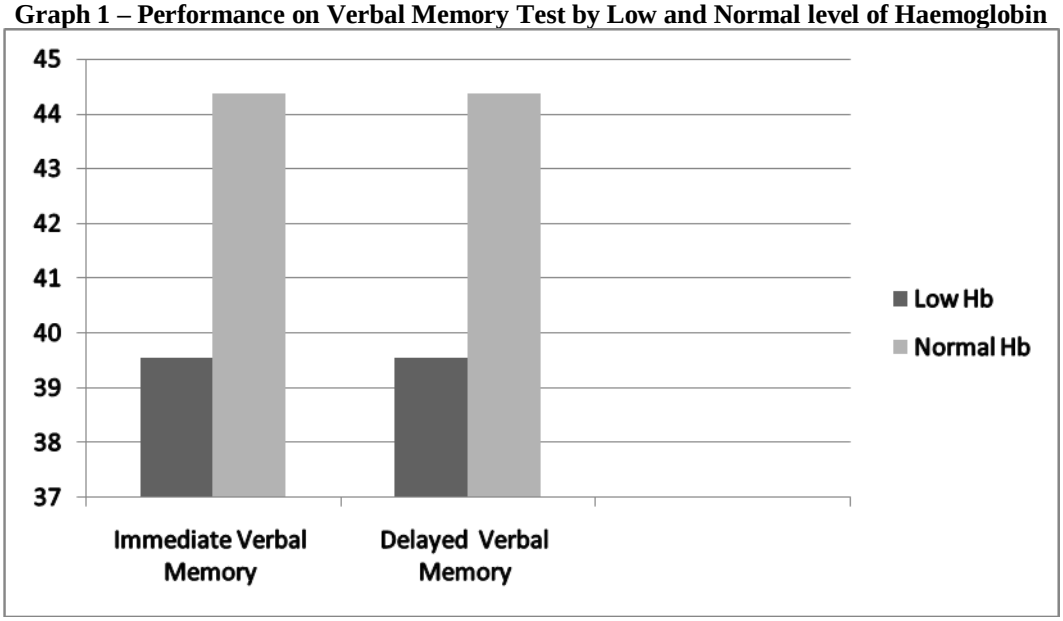
Table 1.2 – Performance on Verbal Memory Test by Low and Normal level of Haemoglobin

		Mean	t	p
Immediate Verbal Memory	Low Haemoglobin	39.56 ± 2.60	-17.251	0.000 *
	Normal Haemoglobin	44.36 ± 2.22		
Delayed Verbal Memory	Low Haemoglobin	39.56 ± 2.60	-17.251	0.000 *
	Normal Haemoglobin	44.36 ± 2.22		

* $p \leq 0.01$ Statistically Significant

The Immediate and delayed Verbal memory scores in the normal haemoglobin group were higher than the low haemoglobin group and the results were statistically significant. (p=0.000)

Graph 1 – Performance on Verbal Memory Test by Low and Normal level of Haemoglobin



V. Discussion

The most widely acknowledged Psychophysiological change due to ageing is a decline in cognitive processes. However, not all cognitive processes equally decline with age; this is particularly true with regards to the various faculties of memory. Under this premise, and with these observations in the backdrop this study was designed to explore the various domains of memory functions among the older adult subjects living in Chennai and aged between 50 – 65 years with varying levels of hemoglobin.

Only a limited number of studies have compared adults across the entire range of adulthood on measures of cognitive functioning. Nevertheless, studies conducted in Chennai involving elderly adults with mean ages of 60 or older are uncommon. The available studies are consistent in finding that increased age to be associated with more negative cognitive changes (Salthouse.T, 2011). In our study we were also able to obtain similar results. We were able to observe that low haemoglobin levels are related to decrements in specific domains of memory, the basis of this differential effect is uncertain; our findings are consistent with previous studies that observed anaemia to be associated with low performance on psychological tests.

The pathophysiology of hypoxia induced damage to neuropsychological functions are complex; even as the cerebral levels of adenosine tri phosphate (ATP) are not impaired; the turnover of several other neurotransmitters are altered by mild hypoxia. Acetylcholine synthesis reduces proportionally to the reduction in carbohydrate oxidation; this study was able to document changes in cognitive functions related to lower hemoglobin levels.

In this study we were able to document statistically significant difference in the age-related declines in several major cognitive abilities. The mechanisms that links lower hemoglobin levels to worse global cognition are not understood and require further exploration. Low hemoglobin may be a marker for the presence of conditions such as ischemia (via cerebrovascular disease), hypoxia (via hypoxia-inducible factor and erythropoietin levels) and / or oxidative stress (via iron dysregulation).

Erythropoietin receptors located in the brain has a neuro protective effect; lower erythropoietin levels increases the risk of neuronal degeneration in certain cognitive pathways. Hypoxia explains the alterations in mental function in patients with cardiac or pulmonary failure. Hypoxia impairs brain function by incompletely defined mechanisms. Mild hypoxia impairs memory and judgment, decreases acetylcholine (ACh) synthesis, thus the explanation of the brain's sensitivity to decrease in oxygen availability must include the alterations in the metabolism of the amino acid neurotransmitters as well as acetylcholine (Gary E. Gibson; 1981)

Even as the shrinkage of brain volume with increased age is well-documented, reasons for age-related decreases in brain volume are not fully understood. Multiple factors like Loss of neurons, shrinkage of the dendritic arbor and of cell bodies, decrease in the synaptic density, loss of glial cells, reduction of myelination, and possibly decreases in vascularisation contributes to reduced brain volume (Salthouse.A ; 2011)

As a risk factor for functional and cognitive decrease, the contribution of Anaemia to morbidity and mortality and to a negative effect on quality of life in the elderly is significant. Mild anaemia is an independent risk factor for executive function impairment among older adults. It leads to neurological complications including impaired cognitive function, functional impairment and fall. We were able to observe impairment of cognitive functions in the elderly with reduced haemoglobin level, in par with the results obtained by David L et

al. (2003). Denny S. et al (2006) have found that anaemia is strongly associated with poorer cognitive function ($P = .0001$), and could even predict a decrease in it over a four year period.

Chaves, P. H et al (2006) reported that the association between mild anaemia and a greater likelihood of having executive function impairment in non demented community-dwelling older adults without advanced physical disability to be strong and independent. Reasons cited included the chronic reduction of cerebral oxygenation secondary to decreased oxygen carrying capacity of the blood due to anaemia; negative effect of anaemia on physical function and conditioning.

Atti AR et al (2006) have demonstrated that the risk of dementia was higher in the presence of anaemia among older adults and anaemic individuals with normal mental status were more likely than non-anaemic patients of the same age to develop dementia over 5 years. Similar to our results Zamboni Vet al (2006) also reported an increase in the risk of cognitive dysfunctions in older individuals even with mild anaemia.

The study done by Valentina Z et al (2006) among a sample of elderly with the mean age of 72.0 years found that the participants with cognitive impairment presented with a higher prevalence of anemia (47%) compared to those without cognitive impairment (35%, $p < 0.001$), that study also found that low hemoglobin levels were significantly associated with cognitive impairment. We were also able to observe that low hemoglobin levels are independently associated with cognitive performance in older adults. Raj C. Shah et al (2008) conducted a study among a cohort of older adults and were able to find an association between normal and low hemoglobin concentrations with specific measures of cognitive function; this is in par with our results suggesting that low hemoglobin concentrations are associated with reduced cognitive functions.

VI. Conclusion

Our work suggests that low haemoglobin levels are to be considered as a potential contributing factor among older adults being evaluated for cognitive impairment, the ability to translate a unit change in the cognition measures into terms that are useful for clinical practice would require further investigation. In this study, we were able to observe that lower haemoglobin levels were associated with decreased cognitive functions in the domains of immediate and delayed verbal memory.

VII. Limitations Of The Study

The major limitation of analyses with cross-sectional data is that all of the observations are collected at the same point in time, and thus models with different directions of causal relations are not easily distinguished, Unfortunately, relatively little is currently known about the dynamics of changes in either brain or cognitive variables, or about the lags between changes in the two types of variables, and therefore two-occasion longitudinal information (and information from related cross-lagged panel analyses) may be of limited value for distinguishing temporal order among variables. The structural and physiological characteristics such as cortical thickness, cerebral blood flow, concentration of brain metabolites, quantity of neurotransmitters or receptor sites, number of neurons, density of synapses or spines, were not considered in this study.

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