Impaired Executive Functions among Anaemic Elderly

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ABSTRACT:

Background: Executive cognitive function is one's ability to think abstractly, plan, initiate, sequence, monitor, and stop complex behavior. Executive cognitive dysfunction can precede the memory disturbances of dementia and that deficits of executive function are present in many chronic disorders and are incriminated in negatively affecting activities of daily living. Anemia is a common disorder in the elderly claimed to affect their executive function. **Objective:** We studied relationship between anemia and executive dysfunction among the elderly. **Method:** Eighty elderly patients were recruited and divided into 2 groups: 40 anemic compared to a matched group of 40 non-anemic. Both groups were subjected to MMSE (Mini-mental state examination), ADL (Activities of daily living) and IADL (Instrumental activities of daily living), Verbal fluency and contrast programming tests. Laboratory investigations were done including CBC (complete blood count), iron profile, liver function and kidney functions. **Results:** Anemic group performed worse than control group regarding their executive function tests with statistically significant difference when using contrast programming (p value=0.01), with worse results among male cases than females and the difference was statistically significant regarding contrast programming test (p value=0.03). Anemic group perform worse on their ADL and IADL than controls with statistically significant difference through their IADL (p value 0.03). **Conclusion:** Anemia could be considered a cause of executive dysfunction among the elderly, and this may contribute to deficits in their ADL and IADL. So we recommend that assessment of executive functions should be a routine measure when evaluating and follow up anemic elderly. Also early diagnosis and proper management of anemia may postpone or prevent impairment in activities of activities of daily living.

Key words: Executive Functions, Anemia, Elderly.

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INTRODUCTION

As defined by DSM-IV, "executive function" is one's ability to think abstractly and to plan, initiate, sequence, monitor, and stop complex behavior[1]. Executive dysfunction can precede the memory disturbances of dementia; people with executive dysfunction can have a normal Mini-Mental State Examination (MMSE) score but still have severe functional limitations[2]. In other word most commonly used cognitive screening instruments, including the MMSE, are insensitive to

executive dysfunction[3]. Although executive impairment is generally associated with dementia, recent studies have suggested that patients with chronic medical diseases may also have executive deficits independent of psychiatric co-morbidities and as executive functions are associated with functional outcomes, medication compliance, and the capacity to give informed consent, it is important to it be assessed[4]. Executive impairment explained 28% of the variance in the performance of activities of daily living in patients with Alzheimer's disease[5] whereas in another study, the rate of change in executive function explained 32% of the variance in the rate of change in the performance of instrumental activities of daily living associated with normal aging[6]. The prevalence of executive impairment in medical inpatient services is high. With the use of published cutoff points, 72% of hospitalized inpatients in medical or surgical services seen by a psychiatric consultation service failed to do well on either of two validated bedside executive function tests[1]. Executive functions have statistically significant effects on both Activity of Daily living (ADL) and Instrumental Activity of daily living (IADL) impairment and this emergent disability is not well detected by traditional global cognitive measures as MMSE evaluation and treatment may be delayed unless executive functions are employed[7].

According to the World Health Organization (WHO) definition of anemia is haemoglobin level of less than 13g/dL for men and less than 12g/dL for women[8]. Studies showed that anemia may increase the risk of cognitive impairment and that anemia is one factor to bear in mind when evaluating risk of incident dementia[9] Moreover mental or psychological changes may precede hematological signs by months or years. This in fact is the initial or only symptoms[10].

So the Aim of the current study was to examine the relationship between anemia and executive dysfunction among the elderly patients.

SUBJECTS AND METHODS

Sampling: 80 elderly patients (60 years and above), both males and females were recruited from the Geriatric inpatient department, Ain shams university hospital. They were divided into two groups according to the WHO definition of anemia. Case group: 40 patients suffering from anemia. The Control group who were 40 patients matched for age and gender with blood picture and iron profile showing that they do not suffer from anemia.

With the following exclusion criteria: no previous history of dementia no medical illnesses which could affect the executive functions as: severe anemia, diabetes mellitus, thyroid dysfunction, cerebro-vascular strokes, hypertension and no psychiatric illnesses as depression, substance abuse, schizophrenia no current intake of drugs which affect the cognitive function as psychotropic drugs. Also elderly with significant physical limitation were excluded.

All patients were subjected to comprehensive assessment including. Detailed history with special consideration to the previous exclusion criteria .Physical examination of the functional status including: assessment of the cognitive status by using the Arabic version of MMSE[3, 11]. MMSE is one of the most commonly used cognitive screening measures because it is quick and easy to

administer, it include specific questions related to attention, orientation, memory, calculation and language. The measure's score is based on 30 total points, and impairment is indicated by a score of 24 or lower. While this measure is often used to screen for memory function, it has a number of psychometric limitations, such as executive function items[12]. Then assessment of the executive function using 2 bed side tests namely: verbal fluency and contrast programming.

Verbal fluency test: used to assess semantic verbal fluency, the animal naming task requires patients to generate the names of as many animals as possible in 60 second. Scores are determined by summing correct responses, with higher scores reflecting better performance[13].

Contrast program test: A test measuring inhibitory control component of executive functions. In this test, the examiner will randomly hold up either one or two fingers; the patient is instructed to do the opposite, i.e., to hold up two fingers when the examiner holds up one or vice-versa. Ten trials are customary; the patient with significant executive impairment will have trouble resisting the inclination to mimic the examiner and will hold up the same number of fingers[14]. Measure of inhibition was most strongly related to IADL integrity[15].

The Arabic version of the Geriatric Depression State (GDS)[16-17] was used for assessment of depression**.** It is the 15-item GDS which is well validated tool often used to screen for depressive symptoms in older individuals. This measure is scored based on a 15-points scale and impairment is indicated by a score of 5 or higher.

Assessment of the activity level performed by: ADL (Activity of Daily living)[18] and IADL (Instrumental Activity of daily living)[19]. Questionnaire of both ADL and IADL are informant based assessment of functional disabilities. The ADL questionnaire measures functionality in 5 areas: bathing, toileting, grooming, dressing and eating. While the IADL questionnaire measures functionality in traveling, shopping, house work, managing finances, using the telephone and taking medications.

Laboratory investigations:

Venous sampling was collected by venepuncture and the sample was used for measurement of: CBC**.** Iron profile including serum iron, serum ferritin. CBC: 1ml of venous blood on EDTA (using coulter counter with microscopic examination of leishman stained peripheral blood smears). Serum Ferritin was measured by a two site immuno-luminometric assay (by k Sangtec Diagnostica). Also kidney function and liver functions were done.

Statistical methods:

Data entry and analysis were done with the program SPSS (Statistical Package for Social Science) version 15.0. The statistical tests used in the analysis are Student T test, Chi-square test, Pearson Correlation Coefficient and Spearman's correlation coefficient.

RESULTS

The study sample is composed of 80 elderly patient 40 males and 40 females. Cases and control were matched with no statistically significant difference regarding age, sex and years of education as well as presence of different chronic medical disorders

which may impair the executive cognitive functions. By comparing both cases regarding their socio-demographic data, it was found that mean age of cases was higher (70.2±6.8 years) than the control group (67.6±6.5 years), and the difference was not statistically significant (p value=.08). Regarding educational level more than 70% among each group were illiterate with p value 0.5, statistically not significant. There was a lower mean HB among cases (9.3±2.2g/dl) compared to controls (12.1±2.0g/dl) and the difference is highly significant statistically (p=0.000), also lower serum ferritin among cases (98.5±165.4g/dl) compared to controls (227±199.6g/dl) and the difference is highly significant statistically (p value= 0.002).

Comparing performance on executive functions between cases and control showed that cases had a lower mean scores of MMSE, verbal fluency and C-program however the difference was statistically significant regarding contrast programming as seen in table (1).

Comparing cases to control regarding performance on ADL revealed that the number of assisted patients among cases exceeded that among control however the difference was not statistically significant as in table (2). Cases where then compared to control regarding IADL. Number of assisted patients among cases significantly outnumbered that of control as in table (2) (p=0.02).

Among cases males had significantly worse scores on contrast programming when compared to females as in table (3).
There is no significant difference statistically between males and females patient as regards MMSE or the Verbal fluency mean score. There is a lower mean of C-Program among male cases compared to female cases and the difference is statistically significant (P<0.05).

Lower HB and serum iron levels were more among males yet the difference was not statistically significant as in table (4).

Cases were divided on basis performance on ADL and I ADL into assisted and independent. Comparison on mean scores of executive functions showed that the assisted group (on ADL and IADL) had worse scores on executive functions yet the difference is not statistically significant as seen in tables (5 and 6).

Table (1) Comparison between cases and controls as regards performance on MMSE and both tests f executive function (verbal fluency and contrast program):

	Cases		Control		T	P
	Mean	SD	Mean	SD		
MMSE	27.4	1.3	27.8	2.0	1.1	0.4
Verbal fluency	6.7	2.1	6.9	1.8	0.4	0.2
C Program	7.0	2.3	8.0	1.3	2.4	**0.01***

P<0.05 Significant

Table (2) Comparison between cases and controls as regards ADL and I ADL

	Cases (N=40) No. %	Control (N=40) No. %	X2	P
ADL				
Independent	24 60.0	29 72.5	2.8	0.2
Assisted	16 **40.0**	10 25.0		
Dependent	0	1 2.5		
IADL				
Independent	14 35.0	25 62.5	7.7	**0.02***
Assisted	26 **65.0**	14 35.0		
Dependent	0	1 2.5		

Table (3) Comparison between males and females cases as regards MMSE and both tests f executive function (verbal fluency and contrast program):

	Males (N=20) Mean SD	Females (N=20) Mean SD	t	P
MMSE	27.5 1.4	27.3 1.1	0.4	0.6
Verbal fluency	6.35 1.8	7.05 2.4	1.0	0.3
C-Program	6.2 1.9	7.8 2.8	2.2	**0.03***

* P<0.05 significant

Table (4) Comparison between males & females cases regarding Hb and iron level

	Males (N=20) Mean SD	Female (N=20) Mean SD	T	P
Hb	8.8 2.4	9.9 1.8	1.5	0.1
Iron	38.1 29.2	38.2 25.8	0.01	0.9

P>0.05 not significant

Table (5) Comparison between independent and assisted cases (ADL) regarding MMSE and both tests f executive function (verbal fluency and contrast program):

ADL	Independent (N=24) Mean SD	Assisted (N=16) Mean SD	T	P
MMSE	27.5 1.2	27.2 1.3	0.5	0.5
Verbal fluency	6.7 2.1	6.5 2.2	0.3	0.7
C-Program	7.2 2.2	6.6 2.6	0.8	0.4

P>0.05 not significant

Table (6) Comparison between independent and assisted cases (IADL) as regards MMSE and both tests f executive function (verbal fluency and contrast program):

IADL	Independent (N=14) Mean SD	Assisted (N=26) Mean SD	T	P
MMSE	27.4 1.5	27.3 1.2	0.09	0.9
Verbal fluency	7.2 1.8	6.3 2.2	1.3	0.1
C-Program	7.7 2.1	6.6 2.4	1.4	0.1

P>0.05 not significant

When correlating between ADL and IADL performance on one side and measures of executive function showed no significant correlation. This was also true on correlating ADL to HB and iron levels as seen in table (7).

Table (7) Spearman's Correlation coefficient between ADL and IADL on one side HB, serum iron and global and executive cognitive functions

	ADL	IADL
MMSE	r=-0.094 P=0.5	r=-0.016 P=0.9
Verbal fluency	r=-0.052 P=0.7	r=-0.200 P=0.2
C-Program	r=-0.130 P=0.4	r=-0.222 P=0.1
HB	r=0.143 P=0.3	r=-0.022 P=0.8
Iron	r=0.173 P=0.2	r=0.110 P=0.4

P>0.05 not significant

DISCUSSION

The identification of potentially modifiable risk factors for executive function impairment in relatively healthy older adults could ultimately contribute to the development of novel preventive opportunities aimed at the maintenance of autonomy in older ages. Few Previous studies investigated anemia as a risk factor for executive dysfunction with various results[20-21]. The elderly are more at risk of developing executive dysfunction and are also more likely to suffer from anemia, although there are relatively few studies addressing this association[9].

The current study compared a group of anemic elderly to non anemic elderly group matched for age, sex, educational level and co morbidity with other medical problems. Low MMSE scores below the cut off point were excluded to rule out dementia. Depressed patients were also excluded. This was followed by correlation analysis between executive functions, parameters of anemia and activities of daily living (ADL) and instrumental activities of daily living (IADL). Verbal fluency and contrast programming were the two tests selected to assess inhibitory control and retrieval of semantic knowledge components of executive functions. These tests were selected as they measure two different aspects of executive functions as well as being simple to apply bed side tests suitable for illiterate patients who constitute most of the studied group.

Comparing anemic to non anemic patients there was no significant difference between both groups regarding MMSE scores; yet the anemic group had lower mean MMS scores.

There was no statistically significant difference regarding verbal fluency yet the anemic group had significantly worse

scores on contrast programming compared to non anemic group. In a previous study on the same age group, anemia was strongly associated with cognitive functions measured using the Short Portable Mental Status Questionnaire (P=.0001) and demonstrated the association between anemia and possible cognitive impairment[22-23].

In a previous study, 1435 non demented subjects aged 75-95 years were followed up for 3 years to detect incident dementia cases[22] (DSM-III-R criteria). Subjects that fulfilled WHO criteria for anemia, baseline HB concentration; 13g/dL (men) and 12g/dL (women), had a higher hazard ratios (HR) of developing dementia 3 years later (HR 1.6, 95% CI: 1.1-2.4). In persons with good baseline cognition (MMSE>or=26, n=1139), the association was stronger and still significant after adjustments for conditions potentially related to anemia and dementia, such as chronic diseases, inflammatory markers, and indicators of nutritional status. The HR was increased even when different HB cut offs for anemia definition was used. The study concluded that anemia is suggested to be a new potential modifiable risk factor for dementia.

The study using MMSE to assess the cognitive capacity of the participants showed that anemic compared to non-anemic had significantly higher cognitive impairment (p=0.016). Anemia had an independent association with possible cognitive impairment[23].

Cognition and functional status were assessed using measures of selective attention, episodic memory, cognitive flexibility and instrumental and basic activities of daily living among 4,068 individual aged 65–84 years, all persons with mild anemia defined according to WHO criteria and mild grade anemia was defined as a HB concentration between 10.0 and 11.9g/dL in women and between 10.0 and 12.9g/dL in men. Mild anemic elderly persons had significantly worse results on almost all cognitive and functional measures[24].

In another study, mild anemic performed worse than non anemic elderly individuals on all tests of cognitive function however, most differences were no longer significant once adjusted for demographic and clinical confounding factors[25]. In our study we tried to control possible confounding factors matching cases and controls regarding all socio-demographic variables. Most of the studies agree on the association between anemia and impaired executive functions yet the degree of correlation depends on which aspect of executive function is being assessed in addition to multiple methodological differences[9].

Functional disability was found to be significantly associated with anemia of any grade in 3 community-dwelling studies[26-27]. No differences in instrumental and basic ADL were found between anemic and non anemic elderly persons in a Japanese population living in the community Post-hoc analysis seems to suggest that higher level of IADL disability could be associated with mild anemia[28]. In our study the rate of impairment on IADL was significantly higher among anemic patients. More anemic patients were impaired on ADL yet the difference was not statistically significant. The association between anemia and functional disability may have few explanations. One of which being through the negative impact anemia exerts on executive functions however inferring a definite causative correlation is beyond the

scope of this paper. Executive functions as a factor contributing to functional disability is an area that still needs a lot of research. One explanation for the recurrent finding underscoring executive functioning is that it reflects a complex domain encompassing multiple cognitive components, such as working memory, inhibition, sequencing, generation, and planning. Thus, it is important to parcel out specific elements of executive functioning with more precise measures to determine elements that are most salient to functional changes.

Based on the results of the current study males had significantly worse scores on contrast programming as well as lower mean score on verbal fluency results which is similar to previous studies[23, 29].

A recent study compared the contribution of impairment in executive function or global cognitive function to predicting functional decline compared level of functional difficulty ADLs and IADLs at baseline and at 6-year follow-up and survival at follow-up. The association was independent of age, education, depression, medical co morbidities, and baseline functional ability. Compared to women with no impairment, women with executive function impairment had significantly worse ADL and IADL function cross-sectional and over 6 years. Another study assessed the relevance of multiple elements of executive functioning to instrumental functional abilities Response inhibition was most strongly related to IADL integrity[15].

CONCLUSION

Anemic elderly perform worse on their MMSE, and on both tests of executive function (verbal fluency and contrast program) and the results were worse among males with statistically significant difference regarding contrast program test. Males perform worse than females through the three tests with statistically significant difference also regarding contrast program.

RECOMMENDATIONS

Based on the results of the current study, executive function should be evaluated routinely among anemic elderly. Further studies especially longitudinal ones are needed for more explanation of the causative relationship between executive cognitive dysfunction and anemia.

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