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DELIRIUM OUTCOMES AND ITS RELATION TO NUTRITIONAL STATUS IN ELDERLY PATIENTS ADMITTED TO ACUTE GERIATRIC MEDICAL WARD

W.M. Abd-El-Gawad[1], R.M. Abou-Hashem[1], M.O. El Maraghy[2], G.E. Amin[3]

Abstract: *Background and Objectives:* Malnutrition is a prevalent and under diagnosed problem among elderly and it is considered as a major risk for delirium. So, the primary aim was to clarify the effect of nutritional status on delirium and its outcomes: length of stay (LOS), and three month mortality, in recently hospitalized elderly patients. *Method:* A prospective cohort study was conducted on 190 patients aged 60 and over admitted to acute geriatric medical wards. Patients were subjected to screening for delirium using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria and nutritional assessment using Mini Nutritional Assessment-Short Form-Arabic version (MNA-SF-A) score, serum prealbumin, total protein (TP), and albumin. *Results:* Mean age was 68.72±7.60 years. Delirium prevalence was 17.6% (n=21). Three month mortality and median LOS were significantly higher in delirious than non-delirious patients (p= 0.003, 0.002 respectively). Delirious patients had statically significant lower MNA-SF-A scores, prealbumin, TP, albumin levels (p=0.028, <0.001, 0.037, 0.033 respectively) than non–delirious patients. By regression, delirium was predictor of the three month mortality (Odds Ratio=1.314, p value=0.022) and delirium and TP were predictors of increased LOS (β= 4.059, 1.655, p value=0.020, 0.019). MNA-SF-A scores, TP, albumin, and prealbumin levels were predictors of delirium (β=0.251, 0.592, 1.012, 0.448, p value=0.025, 0.034, 0.016, <0.001). *Conclusion:* Delirium is an independent predictor of increased length of stay and three month mortality. MNA-SF scores, total protein, albumin and prealbumin levels are independent predictors for the occurrence of delirium in hospitalized elderly patients.

Key words: Nutrition, delirium, mortality, length of stay, MNA-SF-A.

Introduction

Elderly population is a rising problem all over the world. In Egypt, 7.3% of the population in 2011 are elderly aged 60 years and over and it is expected to reach 11.6% in 2030 (1).

Delirium is a common and serious problem affecting elderly people especially with multiple chronic diseases. Delirium affects 11-42% of medically ill patients (2) and it is associated with many adverse outcomes such as functional and cognitive impairment (2, 3).

Malnutrition is a prevalent and frequently undiagnosed problem among hospitalized elderly patients (4). Many diseases can lead to subclinical catabolic and inflammatory state (5). This leads to protein catabolism which adversely affects serum proteins levels and anthropometric parameters resulting in malnutrition which is considered a major risk for delirium (5, 6).

The significance of any association between malnutrition and delirium in acutely hospitalized elderly patients is poorly articulated in literature, despite widespread interest on addressing malnutrition as a risk factor for delirium (5).

So, the primary aim of the present study was to clarify the effect of nutritional status on delirium and its outcomes; length of stay and three month mortality; in recently hospitalized elderly patients in acute geriatric medical ward.

Method

Setting and participant

A prospective cohort study was conducted on 190 patients aged 60 years and over admitted from March 2011 to October 2011 to the acute geriatrics medical ward of Geriatrics and Gerontology department in Ain Shams

1. Geriatrics and Gerontology department, Faculty of Medicine, Ain Shams University, Cairo, Egypt; 2. Clinical pathology department, Faculty of Medicine, Ain Shams University, Cairo, Egypt; 3. Environmental and Occupational department, Faculty of Medicine, Ain-Shams University, Cairo, Egypt.

Corresponding Author: Dr Wafaa Mostafa Abd-El-Gawad, Geriatrics and Gerontology department, Faculty of Medicine, Ain Shams University, Abbassia, Cairo, Egypt, E-mail: wafaager@hotmail.com. wafaager@med.asu.edu.eg, Telephone: +201002863434.

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University hospitals. For the purpose of the study, patients were excluded if they developed incident delirium during hospitalization or had history of cognitive impairment, drug toxicity, substance abuse, or on medications that could affect cognition. The study had been approved by the ethical committees of Geriatrics and Gerontology department. Informed consent was obtained from all patients or next kin.

Data collection

Data were collected on personal characteristics, co-existing chronic medical illness, clinical features, and laboratory results. Exclusion of cognitively impaired patients was confirmed after resolving of delirium using the Arabic version of Mini-Mental State Examination (MMSE) (7). A cut-off of less than 24 has 85% sensitivity and 98% specificity (8).

Diagnosis of delirium

The diagnosis of delirium was based on adequate clinical history taking with special focus on any recent change in conscious level, cognition, and function in addition to the application of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria which is considered the gold-standard for diagnosing delirium. It is very sensitive particularly among acutely ill and hospitalized patients (9). This assessment was performed within the first 24 hours of presentation.

Nutritional assessment

It was done using Mini-Nutritional Assessment-Short Form Arabic version (MNA-SF-A) score (10). It scored as normal if patient got 12–14 points, at risk of malnutrition if scored 8–11 points and malnourished if scored 0–7 points. Data collection was taken from patient or family member. Anthropometric measures such as body mass index (BMI), mid arm circumference (MAC), and calf circumference (CC) were also performed.

Laboratory investigation

5 mL venous blood were collected from each participant, and divided into 2 tubes: 2.5 mL on EDTA-tube for complete blood count (CBC) and 2.5 mL in a plain tube for chemical analysis. CBC was done on Beckman Coulter LH 750 automated cell counted (Beckman Coulter Inc, California, USA). TP, albumin, cholesterol, and triglyceride, were assayed on Synchron CX9 autoanalyser (Beckman Inst. Inc., California, USA) using the manufacturer's reagents. Prealbumin was measured by Human Prealbumin ELISA kit (Immunology Consultants Laboratory, Oregon, USA), which is a sandwich enzyme-linked immunosorbent assay.

Outcome Variables

The outcomes variables were prolonged length of stay (PLOS) (11), hospital length of stay (LOS), and three month mortality. A follow-up visit was done 90 days after each patient's entry into the study to assess the mortality.

Statistical Analyses

All data analysis was performed using the 16th version of SPSS (Statistical Package for Social Science). In comparing between 2 groups; qualitative data were analyzed using Pearson's chi-square test or Fisher's Exact test and quantitative data were analyzed using student t-test or Mann–Whitney test. Correlations between two quantitative variables were done using Spearman's correlation tests. For outcomes of interest (LOS and three month mortality), generalized linear models were used to detect if delirium or any of nutritional parameters were predictors for increased LOS and three month mortality. In addition, generalized linear model was used to detect the effect of nutritional parameters as predictors for the occurrence of delirium.

Results

A total of 190 patients aged ≥60 years were recruited. Of these, 119(62.6 %) patients were included, and the other 71(33.4%) patients were not reviewed based on the exclusion criteria noted previously.

In our study, mean age was 68.72±7.60 years old. Delirium prevalence was 17.6% compared with 82.4% patients who were never delirious. Delirium was significantly more prevalent among males than females (p value <0.001). Delirious patients also had significantly longer LOS (p value=0.002), lower MNA-SF-A scores, prealbumin, TP, albumin levels, and higher WBCs count (p=0.028, <0.001, 0.037, 0.033, 0.002 respectively) (Table 1, 2).

Three month mortality was significantly higher in males than females and in delirious patients (p value=0.048, 0.003 respectively). Died patients had lower MNA-SF-A scores, MAC and albumin levels (p-value=0.006, 0.009, 0.004) (Table 1, 2). LOS was positively correlated with number of comorbidities, WBCs count and negatively correlated with MNA-SF-A scores, TP, albumin and total cholesterol levels (Table 3).

By regression, delirium was the only predictor of the three month mortality (Odds Ratio=1.314, CI= 0.186-2.442, p value=0.022) after adjustment of age, sex, number of comorbidities, MNA-SF-A scores, MAC, WBCs count,

Table 1

General description of patients' characteristics of studied population with comparison between males and females

Variable	Males (n=64) Mean ± SD	Females (n=55) Mean ± SD	Total (n=119) Mean ± SD	P value Males vs females
Age (yrs)	69.62±8.28	67.67±6.66	68.72±7.60	0.262
LOS**	12(7-15)	10(7-13)	10(7-14)	0.300
PLOS, % (n)	28.1% (18)	18.18% (10)	23.53% (28)	0.269
No. of comorbid diseases*,**	4(3-5)	3(2.75-4.25)	4(3-5)	0.014
Delirium, % (n)	29.7% (19)	3.6% (2)	17.6% (21)	<0.001
MNA-SF-A score	7.08± 2.78	8.67±2.77	7.82±2.88	0.002
• Normal%	6.3% (4)	16.4%(9)	10.9%(13)	
• At risk%	37.5%(24)	58.2%(32)	47.1%(56)	0.002
• Malnourished %	56.3%(36)	25.5%(14)	42%(50)	
Anthropometric measures:				
• BMI	24.15±6.87	30.81±8.85	27.20±7.91	<0.001
• MAC (cm)	26.03±3.82	29.04±6.66	27.42±5.48	0.004
• CC (cm)	34.48±5.45	35.44±8.85	34.92±8.65	0.549
Laboratory investigation:				
• WBCs (103 /cmm) **	8.40(5.92-10.98)	6.00(5.05-8.00)	6.90(5.30-9.70)	0.003
• Lymphocytes(103 /cmm)**	1.41(1.10-2.00)	1.80(1.93-2.10)	1.58(1.10-2.00)	0.028
• Haemoglobin (g/dl)	11.87±2.88	11.06±1.87	11.49±2.84	0.121
• Total protein(g/dl)	6.40±1.16	6.84±0.78	6.60±1.02	0.017
• Albumin(g/dl)	3.10±0.72	3.14±0.60	3.11±0.66	0.971
• Prealbumin (mg/dl) **	7.75(5.50-9.88)	7.5(5.88-11.00)	7.5(5.50-10.50)	0.405
• Total cholesterol (mg/dl) **	136(111-172)	161(112.25-208.50)	140.5(111.25-184.75)	0.095
• Triglycerides (mg/dl) **	79(56-107)	104(71-128)	92(61.25-116.75)	0.019
Three Month Mortality % (n)	26.66%(17)	16.36%(9)	21.85%(26)	0.223

LOS: Length Of Stay, PLOS: Prolonged Length of Stay, MNA-SF-A: Mini Nutritional State-short form-Arabic Version, BMI: Body Mass Index, MAC: Mid Arm Circumstances, CC: Calf Circumference, WBCs: white blood cells; *No. of comorbid disease: include diabetes mellitus, hypertension, ischemic heart disease, congestive heart failure, chronic liver disease, chronic kidney disease, cancer, rheumatological diseases; ** By Mann Whitney test, median and interquartile ranges were used. p-value is significant if <0.05.

Table 2

Comparison between delirious and non-delirious patients and three month alive and died patients

Variable	Delirium			Three Month Mortality		
	Delirious(n=21) Mean ± SD	Non-delirious(n=98) Mean ± SD	p value	Died(n=26) Mean ± SD	Alive(n=93) Mean ± SD	p value
Age (yrs)	70.71±9.14	68.30±7.22	0.265	67.00±6.47	69.54 ±7.92	0.171
Sex, males, % (n)	90.5% (19)	45.9% (45)	<0.001***	65.38% (17)	50.54%(47)	0.048
LOS**	13 (9-22.5)	10 (7-13)	0.002	14 (7-22.5)	10 (7-13)	0.223
PLOS, % (n)	47.6% (10)	18.36% (18)	0.009***	50.0%(13)	16.13%(15)	<0.001
No. of comorbid diseases*,**	4.5(8.75-21.75)	4(3-5)	0.186	4(3-6)	4(3-5)	0.579
MNA-SF-A score	6.58± 3.18	8.08±2.73	0.028	6.32±2.59	8.19±2.81	0.006
• Normal% (n)	4.8% (1)	12.2%(12)		7.69%(2)	11.82%(11)	
• At risk% (n)	33.3%(7)	50.0%(49)	0.118##	34.62%(9)	50.54%(47)	0.138##
• Malnourished %(n)	61.9%(13)	37.8%(37)		57.69%(15)	37.64%(35)	
Anthropometric measures:						
• MAC(cm)	26.12±4.25	27.70±5.68	0.232	24.80±3.64	28.35±9.93	0.009
• CC(cm)	32.24±5.16	35.44±8.85	0.118	33.11±4.54	35.65±9.93	0.249
Laboratory investigation:						
• WBCs(103 /cmm)**	11.10(7.78-12.55)	6.5(5.09-9.0)	0.002	9.15(5.7-11.8)	6.79(5.2-9.1)	0.075
• Lymphocytes(103/ cmm)**	1.40(0.65-1.58)	1.67(0.625-2.10)	0.078	1.49(0.52-2.0)	1.7(1.1-2.1)	0.153
• Haemoglobin (g/dl)	12.23±3.36	11.36±2.71	0.192	11.48±2.62	11.53±2.75	0.937
• Total protein(g/dl)	6.12±0.78	6.70±1.04	0.037	6.38±1.59	6.62±0.83	0.334
• Albumin(g/dl)	2.83±0.58	3.17±0.67	0.033	2.91±0.85	3.81±0.60	0.004
• Prealbumin(mg/dl)**	5.00(2.88-8.63)	8.5(6-11)	<0.001	8(5.38-10.63)	7.5(5.5-10.5)	0.938
• Total cholesterol (mg/dl)**	120(101-150)	146.5(116-189)	0.387	128(105-171)	143.5(114-191)	0.205
• Triglycerides(mg/dl)**	91.5(69-101)	92.5(57.75-119)	0.712	82(66-121)	93.5(60-116)	0.820
Three Month Mortality % (n)	47.6% (10)	16.3% (16)	0.003***	----------	----------	--------

LOS: Length Of Stay, PLOS: Prolonged Length of Stay, MNA-SF-A: Mini Nutritional State-short form-Arabic Version, MAC: Mid Arm Circumstances, CC: Calf Circumference, WBCs: white blood cells, *No. of comorbid disease: include diabetes mellitus, hypertension, ischemic heart disease, congestive heart failure, chronic liver disease, chronic kidney disease, cancer, rheumatological diseases; ** By Mann Whitney test, median and interquartile ranges were used; *** By Fisher exact; ## By Kruskal-Wallis Test; p-value is significant if <0.05.

prealbumin and albumin. Delirium and TP were predictors of increased LOS after adjustment of age, sex, number of comorbidities, MNA-SF scores, prealbumin, albumin, total cholesterol levels and WBCs counts (Table 4). MNA-SF-A scores, TP, albumin, and prealbumin levels were predictors of delirium after adjustment of age, sex, number of comorbidities, and WBCs count (Table 5).

Table 3
Comparison of Length of stay with quantitative and qualitative variables

Variable	rho	p value
Age (yrs)	-0.060	0.514
No. of comorbid diseases§	0.226*	0.013
MNA-SF-A score##	-0.186*	0.047
• Normal	8(5.5-16)	0.016
• At risk	9(6.25-12)	
• Malnourished	12(7.75-16.5)	
Anthropometric measures:		
• BMI	-0.081	0.383
• MAC (cm)	-0.064	0.798
• CC (cm)	-0.083	0.368
Laboratory investigation:		
• WBCs (103 /cmm)	0.228*	0.012
• Lymphocytes (103 /cmm)	-0.026	0.770
• Haemoglobin (g/dl)	-0.180*	0.050
• Total protein(g/dl)	-0.217*	0.018
• Albumin(g/dl)	-0.261*	0.004
• Prealbumin	-0.025	0.788
• Total cholesterol	-0.260*	0.008
• Triglycerides	-0.016	0.788

LOS: Length Of Stay, MNA-SF-A: Mini Nutritional State-short form-Arabic Version, BMI: Body Mass Index, MAC: Mid Arm Circumstances, CC: Calf Circumference, WBCs: white blood cells; ## By Kruskal-Wallis Test. p-value is significant if <0.05; §No. of comorbid disease: include diabetes mellitus, hypertension, ischemic heart disease, congestive heart failure, chronic liver disease, chronic kidney disease, cancer, rheumatological diseases.

Table 4
Generalized linear model for the predictors of the length of state (LOS)*

		95% CI		
	β	Lower	Upper	P value**
Total Protein	-1.655	-3.038	-0.273	0.019
MNA-SF-A	-0.304	-0.749	-0.141	0.180
Albumin	-2.087	-4.188	-0.015	0.052
Delirium	4.059	0.630	7.487	0.020
Total Cholesterol	-0.006-	-0.027	-0.015	0.560

*This model was adjusted for age, sex, number of comorbidities, WBCs count; MNA-SF-A: Mini Nutritional State-short form-Arabic Version, CI: confidence interval; **p-value is significant if <0.05.

Discussion

Delirium is under-reported and unrecognized in clinical setting (12). The role of nutritional state on delirium outcomes is poorly studied. To our knowledge, no study assessed the effect of various nutritional parameters on delirium and its outcomes in recently hospitalized patients.

Table 5
Generalized linear model for the predictors of Delirium*

		95% CI		
	Odds Ratio	Lower	Upper	P value**
Intercept	2.9352	4.569	10.321	<0.001
MNA-SF-A	0.251	0.032	0.470	0.025
Total Protein	0.592	0.045	1.139	0.034
Albumin	1.012	0.186	1.837	0.016
Prealbumin	0.448	0.198	0.697	<0.001

This model was adjusted for age, sex, number of comorbidities, WBCs count; MNA-SF-A: Mini Nutritional State-short form-Arabic Version, CI: confidence interval; **p-value is significant if <0.05.

In this study, delirium prevalence on admission was 17.6% which is similar to previous studies (2, 3, 13). Delirium was an independent predictor for higher LOS which agrees with the majority of previous studies on delirious medical inpatients (14, 15).

This study also confirmed that delirium was an independent risk factor for three month mortality which is similar to the work carried out by Gonzâlez et al (16) and McCusker et al (17). Males showed statically significant higher prevalence of delirium and mortality than females and this was similar to many studies which concluded that male sex is one of non-modifiable risk factors for delirium and mortality in hospitalized elderly patients (18, 19).

There are inconsistent results regarding the association between mortality and delirium. Neither Adamis et al (20), nor Inouye et al's studies (21) found significant increase in 6 month and 3 month mortality respectively even after adjustment of age, sex, dementia, illness severity, and functional status. On the other hand, a large pooled analysis showed that medically hospitalized delirious elderly patients have two to three fold expected mortality than non-delirious patients (from 15 to 37%) (2, 22). Although many researchers have argued that delirium is simply a marker of the severity of illness and comorbidity burden (23), the relationship between delirium and mortality has been shown to be persistent even after adjustment of these factors (17).

Delirium was also associated with poor nutritional parameters which agrees with Culp and Cacchione's study in long term care who found delirious patients had significantly lower albumin and prealbumin protein levels compared to non- delirious (24).

Both poor nutritional state and aging are associated with increased production of cortisol and proinflammatory cytokines that could provoke severe inflammation in the brain and disturb the synthesis and release of many neurotransmitters leading to precipitation and persistence of delirium (25, 26). Many diseases such as coronary heart diseases and its equivalents, diabetes, and chronic liver disease, are very common in elderly and have an influence on their diet

(27). In addition, subclinical catabolic and inflammatory states present in association with chronic diseases lead to an increased production of catabolic cytokines, increased muscle catabolism, and decreased appetite (6, 28). Decreased metabolic reserve of muscles due to age related loss of muscle mass results in a reduced ability to cope with any stress. Subsequently, even minor stress of short duration can unfavorably affect the nutritional status of elderly persons (6, 29) .

Strength and limitations

To our knowledge, this study is the first study addresses the effect of nutritional parameters on delirium and its outcomes in acute care setting. Our sample includes only patients with prevalent delirium due to pure medical cause with intact cognition. We also followed the patients for further 3 months for mortality.

The limitations of the study include small sample size, and inadequate control of the severity of illness.

Conclusion

Delirium is an independent predictor of increased length of stay and three month mortality. MNA-SF-A scores, total protein, albumin and prealbumin levels are independent predictors for the occurrence of delirium in hospitalized elderly patients.

Recommendations

In view of our results, this study highlights the importance of routine nutritional screening in hospitals especially in elderly because it could prevent the occurrence of delirium and its poor outcomes.

Conflict of Interest: The authors have no financial interests or any other kind of conflicts related to the material in the manuscript.

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