Hospital Acquired Depressive Symptoms in Frail Elderly Patients and Its Associations with Zinc Level

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ABSTRACT

Introduction: Frailty is obscure and under-estimated, starts subclinically in elderly who seem to be healthy. Minimal thesis in literature handled the relationship between frailty and depression. The elderly are more subjected to depression and trace elements insufficiency than others.

Objective: To assess newly developed depressive and anxiety symptoms in frail elderly admitted to Ain Shams University (ASU) hospitals and the prevalence of zinc deficiency among them.

Methods: A cross-sectional study was conducted among 90 older frail inpatients. Hospital-acquired depressive and anxiety symptoms were confirmed using the hospital anxiety and depression scale (HADS). Serum zinc level, hemoglobin, and albumin were measured.

Results: There was a significant statistical association between depressive and anxiety symptoms and low serum level of zinc ($p<0.001$).

Conclusion: There is a strong association between depressive and anxiety symptoms in hospitalized elderly and zinc deficiency.

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1. INTRODUCTION

Frailty is prevalent in the elderly, it is defined as a syndrome of deficient reserve and durability to stressors, due to progressive descend in physiologic systems leading to serious complications.\(^1\)

Insufficiency in micronutrient is common in elders such as zinc which is a risk factor for frailty decreasing fitness, and physical dysfunction.\(^2,3\) It has a major role in mental function, antioxidant system, and metabolism. The body has no obvious zinc storage system, so daily intake of zinc is necessary to maintain a steady-state.\(^4\)

The prevalence of zinc deficiency in adults increased with aging to a maximum of 19.7% by the 8th decade of life.\(^5\) Zinc was associated with better overall physical performance.\(^6\)

Healthcare costs have been reported to be higher in people with depressive symptoms compared to those without it.\(^7\) Among hospitalized older adults, anxiety and depression are associated with risk factors and serious comorbidities. Both conditions show increased risk of functional impairment and in adherence to
Charlson Comorbidity Index (CCI).²¹

-Laboratory investigations including hemoglobin level, serum albumin, zinc level which were measured by colorimetric method. Reference ranges of serum zinc is defined as 46-150 µg/dL, while the values lower than 46 µg/dL is defined as zinc deficiency according to the used kit reference (spectrum diagnostics). Non-fasting blood samples were obtained and stored at optimum temperature till the time of analyses.

Statistical analysis: Quantitative variables were presented as mean and standard deviation. Qualitative data were presented as frequency and proportion and the chi-square test was used to compare the two groups. The level of significance was taken at \( p < 0.05 \), otherwise is non-significant. Data entry and statistical analysis were done using a statistical package for social science (SPSS) version 20.0.

3. RESULTS

In the current study, 90 elderly inpatients were chosen as the study population who were admitted to ASU geriatrics hospital. The mean age is 71.8±7.8 years. Among the studied population, 56.7% were females and 43.3% were males.

Regarding functional status, 21 (23.3%) were independent, 21 (23.3%) were dependent and 48 (53.4%) were assisted using ADL scores. Regarding nutritional status, 43 (47.8%) of them were malnourished, 40 (44.4%) were at risk of malnutrition, and 7 (7.8%) were well nourished using MNA scores.

Regarding hospital-acquired depressive symptoms using HADS, 28 (31.1%) showed negative scores, 23 (25.6%) showed borderline scores and 39 (43.3%) showed positive scores for depressive symptoms. Moreover, 32 (35.6%) of them showed negative scores, 28 (31.1%) showed borderline scores and 30 (33.3%) showed positive scores for anxiety.

As regard frailty assessment, 28 were mild, 25 were moderate, 10 were severe, 19 were very severe and 8 were terminally ill.

There was a statistically significant association between aging and levels of frailty \( (p < 0.001) \). Living alone was more frequent among mild frail cases and less frequent in moderate and severe cases \( (p < 0.001) \).

Anemia, hypoalbuminemia, and zinc deficiency were most frequent in both anxious and depressed participants, followed by mixed and significantly least frequent in non-depressed inpatients \( (p < 0.001) \) (Table 1). Frailty high grades were most frequent in both anxious and depressed participants as revealed by

2. MATERIALS AND METHODS

A cross-sectional study included elderly frail inpatients 60 years and older recruited from ASU Geriatrics hospital from April 2019 to April 2020.

The sample size was calculated using the STATA program, setting the type-1 error \((\alpha)\) at 0.05 and the power \((1-\beta)\) at 0.8. Calculation according to these values from previous studies⁴ produced a minimal sample size of 78 cases.

Exclusion criteria included a history of major mental illness, Patients on anti-depressant therapy or sedatives, Patients who take zinc supplements, dementia patients, non-frail or pre-frail inpatients by Fried criteria, degrees 1 - 4 in the Clinical Frailty Scale (CFS).

Data from each patient was collected including demographic data, past history, and drug history. Frailty was diagnosed using Fried criteria as mentioned by Fried et al.¹³ Cognition was screened using the Arabic version of the Mini-mental state examination (MMSE).¹⁴ Depression was screened on hospital admission by the Patient Health Questionnaire 2 (PHQ-2).¹⁵

Those who are frail using fried criteria, non-depressed using PHQ-2 on hospital admission, and cognitively intact using MMSE were subjected to the following:

-Severity of frailty using CFS that was conducted by Rockwood et al.¹⁶

-Hospital-acquired depressive symptoms using Hospital Anxiety and Depression Scale (HADS)¹⁷ using the Arabic version,¹⁸

-The nutritional state using the Mini Nutritional Assessment (MNA) short form.¹⁹

-Functional assessment using Activities of Daily Living (ADL) scale.²⁰

-The weight of comorbid conditions was assessed by

Depression and frailty have common mechanisms in pathophysiology and the same kinds of outcomes indicating an association between them.⁹,¹⁰ Vashum et al and Swardfager et al have shown an association between low zinc and depression in inpatients.¹¹,¹²

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the current study statistics (Table 1).

Charlson index and zinc had the highest significant diagnostic performance in differentiating both abnormal from both normal/mixed (Table 2) \( p < 0.001 \). Age >73, number of comorbidities >4, drugs >6, Charlson index >6, serum zinc level <44 are highly predictive diagnostic values in predicting anxious and depressed inpatients (Table 2).

4. DISCUSSION

Frail geriatric inpatients are increasing, making the evaluation for frailty an important component of the comprehensive geriatric assessment. The aging world increases the need for health and social care resources.22

As regard frailty and serum zinc level, the current study results about hospitalized frail elderly go hand in hand with studies which revealed that the frail had lower serum concentrations of zinc (\( p = 0.001 \)) compared with women who were not frail in community dwelling.2 Zinc insufficiency is highly common in elders which may lead to a frailty syndrome, this may be due to the effect of insulin-like growth factor (IGF)-1 production or action.23

Elders are subjected to micronutrient deficiency because of difficulty with shopping, meal preparation, and anorexia of aging. This may be an important factor making elders at increased risk of developing frailty and therefore hospitalizations and mortality.24

Depressive symptoms were prevalent in hospitalized elderly and associated with decreased ability to perform ADL.25 Moreover, a study including 92 elders during the first 72 hours of hospitalization revealed that the malnourished patients, according to MNA have associated depression.26

Zinc may modulate depression by modifying the function of particular neurotransmitter systems.27 Zinc treatment has been shown to have an antidepressant effect.28

Frailty grades were higher in both anxious and depressed participants as revealed by the current study statistics. There is an interaction between depression and frailty in elders. Both are associated with a higher prevalence and incidence of the other, and a risk factor for the emergence of the other.29

Lack of Zinc is associated with neuropsychiatric disorders as decreased cognition, inability to learn, and depression.30 The increase in glucocorticoids from the hypothalamic-pituitary-adrenal (HPA) axis leading to depressive symptoms which can be initiated by lack of zinc.31

The strength of our study is that we excluded subjects with other psychiatric problems and dementia that affect the nutritional and functional status which could potentially aggravate the results of zinc level and frailty scales. However, the limitation is that the study measured depressive symptoms, not a major depressive disorder. Inpatients with major depressive disorder have a much higher risk than that carried by high scores on symptom rating scales of depression. Moreover, since serum zinc is closely bound to albumin, lower serum zinc concentration in depression may be related to decreased concentrations of its protein.32 This study didn’t measure trace elements other than zinc as well as insulin-like growth factor 1 (IGF-1).

5. CONCLUSION

There is a strong association between frailty in the elderly, depressive and anxiety symptoms, and, zinc deficiency. Screening

### Table 1. Comparison according to depression and anxiety combination by HADS regarding frailty degree and lab findings

<table>
<thead>
<tr>
<th>Frailty degree</th>
<th>Both normal (N=27)</th>
<th>Both abnormal (N=26)</th>
<th>Otherwise (N=37)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>25 (92.6%)( a )</td>
<td>0 (0.0%)( b )</td>
<td>3 (8.1%)( b )</td>
<td>( &lt;0.001^* )</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (7.4%)( a )</td>
<td>0 (0.0%)( a )</td>
<td>23 (62.2%)( b )</td>
<td>( &lt;0.001^* )</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0.0%)( a )</td>
<td>8 (30.8%)( b )</td>
<td>2 (5.4%)( a )</td>
<td>( &lt;0.001^* )</td>
</tr>
<tr>
<td>Very severe</td>
<td>0 (0.0%)( a )</td>
<td>12 (46.2%)( b )</td>
<td>7 (18.9%)( b )</td>
<td>( &lt;0.001^* )</td>
</tr>
<tr>
<td>Terminally ill</td>
<td>0 (0.0%)( a )</td>
<td>6 (23.1%)( b )</td>
<td>2 (5.4%)( b )</td>
<td>( &lt;0.001^* )</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lab results</th>
<th>Both normal (N=27)</th>
<th>Both abnormal (N=26)</th>
<th>Otherwise (N=37)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>13 (48.1%)( a )</td>
<td>24 (92.3%)( b )</td>
<td>34 (91.9%)( b )</td>
<td>( &lt;0.001^* )</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>7 (25.9%)( a )</td>
<td>25 (96.2%)( b )</td>
<td>31 (83.8%)( b )</td>
<td>( &lt;0.001^* )</td>
</tr>
<tr>
<td>Zinc deficiency</td>
<td>0 (0.0%)( a )</td>
<td>26 (100.0%)( b )</td>
<td>24 (64.9%)( c )</td>
<td>( &lt;0.001^* )</td>
</tr>
</tbody>
</table>

\( ^*p < 0.05 \): Significant (S); \( ^{**}p < 0.01 \): Highly significant (HS)

\( ^* \)ANOVA test. \( ^{**} \)Chi square test. \( ^{***} \)Fisher’s Exact test. *Significant. Homogenous groups by post hoc Bonferroni test had the same symbol (a,b,c)

### Table 2. Diagnostic performance of different variables in differentiating both abnormal from both normal/otherwise in HADS

<table>
<thead>
<tr>
<th>Factors</th>
<th>AUC</th>
<th>SE</th>
<th>( P ) value</th>
<th>95% CI</th>
<th>Cut off</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.785</td>
<td>0.051</td>
<td>( &lt;0.001^* )</td>
<td>0.685–0.885</td>
<td>( \geq 73.0 )</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>0.747</td>
<td>0.053</td>
<td>( &lt;0.001^* )</td>
<td>0.642–0.852</td>
<td>( \geq 4.0 )</td>
</tr>
<tr>
<td>Drugs</td>
<td>0.782</td>
<td>0.049</td>
<td>( &lt;0.001^* )</td>
<td>0.685–0.878</td>
<td>( \geq 6.0 )</td>
</tr>
<tr>
<td>Charlson index</td>
<td>0.852</td>
<td>0.039</td>
<td>( &lt;0.001^* )</td>
<td>0.775–0.928</td>
<td>( \geq 8.0 )</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.672</td>
<td>0.062</td>
<td>0.011*</td>
<td>0.552–0.793</td>
<td>( &lt;10.0 )</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.697</td>
<td>0.054</td>
<td>0.003*</td>
<td>0.591–0.804</td>
<td>( \leq 3.2 )</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.886</td>
<td>0.034</td>
<td>( &lt;0.001^* )</td>
<td>0.819–0.952</td>
<td>( \geq 44.0 )</td>
</tr>
</tbody>
</table>

AUC: Area under curve, SE: Standard error, CI: Confidence interval. *significant
for depression, frailty and associated factors should be routinely done on hospital admission as elderly medical inpatients with depressive symptoms were more likely than those without to be readmitted and had higher inpatient services utilization during the follow-up period, independent of functional and health status.

Ethical considerations: Our study is approved by the ethical committee of the faculty of medicine at ASU. The objective of the study was conducted to the patient. Confidentiality of data was assured and no one had the right to read the patient’s medical information except the main researcher. The research was conducted according to the principles of the Declaration of Helsinki.

CONFLICTS OF INTEREST

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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