Original Article

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Impacts of Trace Elements and Antioxidant Vitamins on Anxiety-Depression Disorders in Children on Dialysis

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ABSTRACT

Background & Objective: Few studies have compared the concentration of trace elements and antioxidants in the serum of depressed and non-depressed as well as children on dialysis with and without anxiety.

Materials & Methods: A prospective cross-sectional research was conducted. Forty children undergoing dialysis were assessed to define the correlation between mean serum levels of Selenium, Zinc, Copper, Manganese, vitamin C, and vitamin E and their deficient levels with mood disorders. The Child Depression Inventory (CDI) and Depression Anxiety Stress Scale (DASS) scorings were applied. According to Scorings, patients were divided into no depression and depression and no anxiety and anxiety disorders groups.

Results: Eighteen hemodialysis and 22 peritoneal dialysis patients were enrolled. The median of age was 11 years. Twenty-two patients (55%) were males. Selenium, copper, and vitamin C deficiencies were found in 32.5%, 15%, and 2.5% of patients, respectively. Anxiety and depression disorders were diagnosed in 82.5% and 67.5% of patients, respectively. No relationship between gender, modality of dialysis, duration from onset of dialysis, serum levels of hemoglobin, blood urea nitrogen, albumin, Zinc, Copper, Selenium, manganese, and vitamin C with anxiety and depression disorders ($p > 0.05$ for all). The severity of depression was higher in hemodialysis versus peritoneal dialysis patients ($P < 0.001$). The Serum level of Vitamin E significantly was higher in depressed in comparison with non-depressed cases ($P=0.02$).

Conclusion: There was no relationship between trace elements and vitamin C serum level and depression or anxiety disorders. An unreported finding was significantly higher level of vitamin E in depressed patients in comparison to those without it.

Keywords: Dialysis, Child, Trace elements, Depression, Anxiety

Introduction

Chronic kidney disease (CKD) is a critical community health issue, with an estimated occurrence rate of 15-74.7 cases per million pediatric populations **(1)**. The literature review shows an increased prevalence of depression in CKD in children under dialysis in comparison with other children **(2).** CKD is a risk factor for psychosocial impairment **(3).** Additionally, depression is associated with greater risk of mortality (2). Although depression has been widely studied in CKD children, few studies have focused on anxiety in dialysis children **(4)**.

Trace element deficiency is common in dialysis children. Low intake due to decreased appetite and increased dialysate loss are the main contributing factors for trace elements deficiency **(5).** A significant increase in toxic trace elements level and a reduction in

essential trace elements in adult hemodialysis subjects compared to healthy individuals was confirmed **(6)**. Recent reviews have confirmed the protective role of selenium against postpartum depression **(7)**. Zinc deficiency is common among adult hemodialysis patients (up to 78 %) **(8,9)**. Severe selenium deficiency could lead to neurodegenerative diseases **(10,11)**.

A prevalence of 10-30% has been reported for clinical depression in patients undergoing hemodialysis **(12)**. Depression and anxiety symptoms have been observed in about 24% and 20% of the adult population undergoing hemodialysis, respectively **(13)**. A recent study confirmed the significant impact of low selenium intake on depressive disorders **(14)**. Selenium and non-enzymatic antioxidants in foods, including vitamins E, A and C have a protective influence against various psychological diseases, such as attention-deficit hyperactivity disorder (ADHD), anxiety, autism, bipolar disorder, and depression **(15)**. Gender seems to have a vital role in the prevalence of anxiety and depression disorders among adults undergoing dialysis. A higher frequency of anxiety and depression was reported in females and males, respectively **(16)**.

To the best of our knowledge, despite the numerous studies on adults, few studies have evaluated trace elements deficiency and its relationship with depression–anxiety disorders in dialysis children. In a cross-sectional study we attempt to prospectively investigate this topic in the peritoneal and hemodialysis sections of a tertiary pediatric care center.

Materials and Methods

A prospective cross-sectional study was done in a tertiary care center at Mashhad University of Medical Sciences, Mashhad, Iran, between 2017 and 2019. A total number of 50 peritoneal and hemodialysis patients aged lower than 18 years were assessed for eligibility. For the patients aged ≥ 6 years written informed consent from parents or the patients were obtained. Finally, 40 patients were included. The Ethics Committee of Mashhad University of Medical Sciences approved the study protocol (ethic code: IR. MUMS. fm. REC.1396.494).

This study consisted of two stages. First, the patients were evaluated for zinc, selenium, manganese, copper, vitamin C, and vitamin E deficiencies. Then, they were asked to answer the items present in the depression anxiety stress scale (DASS) and the child depression inventory (CDI) scorings.

Blood samples (10 ccs) were collected to measure the serum levels of zinc, selenium, manganese, copper, vitamin C, and vitamin E, concurrent with routine monthly blood tests. Serum concentrations < 65 ng/dl for zinc, < 80 ng/dl for copper, < 3 µg/dl for manganese, and < 90 µg /l for selenium were considered deficient levels based on the reference ranges of the laboratory kits used in the study. Vitamin E and C deficiencies are defined as serum levels < 5 µg/l and < 2 mg/l, respectively. The serum levels of copper and zinc were measured using colorimetry (BIOREX (Hungary) and GRAINER (Germany) kits, respectively. The serum levels of manganese were measured using the atomic absorption method (MERCK (Germany) kit. High-performance liquid chromatography (HPLC) using PARSEH CHROMABZAR (Iran) and RECIPE (Germany) kits were employed to measure the serum level of vitamins E and C.

However, water-soluble vitamins and zinc loss through dialysate and dialysis patients are prone to develop and vitamin C deficiencies, their concentration is not measured routinely. Multivitamin mineral supplements containing water-soluble vitamins and zinc are commonly prescribed for dialysis patients **(17,18)**. Water-soluble vitamins zinc and vitamin E supplementation are recommended in CKD patients **(19-21)**.

We routinely recommend Nephrovite® or Nephrotonic® tablets (manufactured by Zahravi Company, Tabriz, Iran) in CKD patients before placing them on dialysis. These supplements contain vitamin E (50 mg), vitamin C (60 mg), and zinc (25 mg). Serum zinc, vitamins E and C were measured to define whether adding these supplements is sufficient to prevent deficient levels. Additionally, we aimed to determine whether their serum levels correlate with mood disorders.

The Child Depression Inventory (CDI) scoring was used to evaluate depression disorders and the Depression Anxiety Stress Scale (DASS) scoring was applied to define anxiety as well as depression disorders. In children younger than 10 years, parents completed the questionnaires. According to the CDI scoring, scores ≥ 22 are defined as depression. Based on the DASS scoring, scores≥ 10 and ≥ 8 are considered as depression and anxiety disorders, respectively. In the DASS scoring, scores 0-9, 10-13, 14-20, 21-27, and > 28 are defined as normal, mild, moderate, severe, and very severe depression disorder, respectively. In anxiety items, scores 0-7 are considered normal. Scores 8-9, 10-14, 15-19, and >20 are defined as mild, moderate, severe, and very severe anxiety disorders, respectively.

According to the CDI and DASS scorings, the following groups were considered: no depression and depression disorders, anxiety and no anxiety disorders. Serum levels of zinc, selenium, manganese, copper, and vitamins E and C were compared between the sub-groups of groups 1 and 2.

Sample size and statistical analysis

According to the enumeration method, 40 of 50 (80%) eligible patients were included. Statistical analysis was done via the SPSS Windows program version 16 (SPSS Institute, Inc., Chicago, IL, USA). Normality was checked using Shapiro-Wilk or Kolmogorov-Smirnov tests according to the sample size. All experimental values are presented as means ± standard deviation (SD), median and interquartile ranges (IQRs), or

percentage (%) and frequency. The chi-square and Fisher exact tests were used to screen the association between quantitative variables. Independent t and Mann-Whitney U tests were used to screen for differences between the groups. Statistical significance was set at $P < 0.05$.

Results

Among the 40 included patients, 22 (55%) were males. The median age of the patients was 11 years (interquartile ranges 8-14). The baseline characteristics of patients are presented in Table 1. Of the 18 hemodialysis (HD) patients, 14 (77.8%) underwent standard dialysis sessions (three 4-hour dialysis sessions). In HD and PD groups, a history of mood disorders was found in 33.3% (n=6) and 27.3 % (n=6) cases, respectively (p = 0.67). Two patients (11.1%) in the HD group had a history of mood disorders in their close relatives. Based on the CDI and the DASS scorings, 42.5% (n=17) and 50% (n= 20) of the participants had depression. Depression disorders were confirmed in 67.5% (n=27) of patients. Anxiety disorders were found in 33 cases (82.5%) based on DASS. Anxiety disorders were reported in 94.5% (n= 17) and 72.7% (n=15) of the girls and boys. Anxiety disorders were found in 88.9% (n=16) and 77.3% (n= 17) of HD and PD cases, respectively. Depression disorders were reported in 66.7% (n=12) of girls and 68.2% (n=15) of boys, 77.8% (n=14) of HD patients, and 59.1% (n=13) of PD patients.

The concentrations of zinc, vitamin E, and manganese were within the normal ranges in all cases. Selenium, copper, and vitamin C deficiencies were found in 13 (32.5%), six (15%), and one (2.5%) patients, respectively. In Total, 38.9% (n=7) and 27.3% (n= 6) of HD and PD patients had selenium deficiency. Copper deficiency was found in 11.1% (n=2) of HD and 18.2% (n=4) of PD patients. The only case of vitamin C deficiency was an HD patient. Neither depression nor anxiety had a relationship with gender and modality of dialysis. In addition, depression and anxiety were as common in patients placed on dialysis from ≤ one year ago the study as > one year ($P > 0.05$ for all) (Table 2).

Serum levels of hemoglobin, blood urea nitrogen (BUN), albumin, zinc, copper, selenium, manganese, and Z scores of height for age were not significantly different in cases with anxiety or depression disorders versus those without ($P> 0.05$ for all) **(Table 3)**. A higher serum level of vitamin E was detected in depressed patients compared to those without ($P=0.02$) (Table 3). Age, duration from dialysis placement, Z score of weight for age, serum levels of iron, vitamin C, and manganese were not significantly different in patients with and without depression, or with and without anxiety disorders ($P> 0.0\ 5$ for all) (Table 4). As reported in **Table 5**, selenium deficiency was more prevalent in boys than in girls (36.4% vs. 27.3%, respectively; $P=0.56$). In addition, it was more prevalent among HD than in PD patients (38.9% vs. 27.3%, respectively; $P= 0.43$). In contrast to selenium deficiency, copper deficiency was more common in girls than in boys (16.7% vs. 13.6%, respectively; $P=0.78$). In addition, it was more frequent in PD than in HD patients (18.2% versus 11.1%, respectively; $P=0.53$).

Selenium deficiency was more frequent in patients placed on dialysis for ≤ one year ago compared to > one year ago (42.8% vs. 26.9% respectively; $P= 0.30$). In contrast to selenium, copper deficiency was more frequent in patients who underwent dialysis from ≤ one year ago compared to > one year ago (7.1% versus. 19.2%, respectively; $P= 0.30$) **(Table 5).** These findings indicate that with more time passing from the onset of the dialysis, the frequency of copper deficiency increased. Although the frequency of depression was not significantly different among HD and PD patients, based on the CDI scoring, the severity of depression was significantly higher in HD than in PD patients (mean score of 24.05±5.57 versus 14.22±9.04, respectively; $P< 0.001$).

Table 1. Baseline demographic and laboratory characteristics of enrolled cases

Variable	N (%)
Male	22(55)
Female	18(45)
Hemodialysis	18(45)
Peritoneal dialysis	22(55)
Etiologies of CKD [1]	
Structural anomalies [2]	25(62.5)
Inherited diseases [3]	6(15)
Idiopathic	5(12.5)
Glomerular diseases [4]	3(7.5)
Tubular diseases [5]	1(2.5)
Variable	**Median(IQR[6])**

Age (year)	11(8-14)
Duration of dialysis (year)	3(1-4)
Z score of weight for age	-0.07(-2.07,+ 1)
Serum iron (µg[7]/dl[8])	58(45.75-74)
Serum Manganese (µg/L[9])	5.9(4.2-8.8)
Serum Vitamin C(mg[10]/L)	5.3(4.22-7.35)
Variable	**Mean ±SD[11]**
Z score of height for age	-0.65± 1.84
Serum urea (mg/dl)	131.6±42.09
Hemoglobin (gr[12]/dl)	11.29±1.61
Serum albumin (gr/dl)	4.19±3.02
Serum Zinc (ng[13]/dl)	94.05±18.68
Serum Selenium (µg/L)	93.13±7.49
Serum Copper (ng/dl)	88.35±13.26
Serum Vitamin E(mg/L)	14.47±3.78

1) Chronic kidney diseases; 2) Renal dysplasia, vesicoureteral reflux, anatomical urinary tract obstructions ; 3) Polycystic kidney diseases, Alport syndrome, familial juvenile nephronophthisis, and cystinosis; 4) Any types of nephrotic syndrome, systemic lupus erythematosus, and rapidly progressive glomerulonephritis; 5) Chronic tubulointerstitial nephritis; 6) Inter quartile range; 7) microgram; 8) Deciliter; 9) Liter; 10) Milligram; 11) Standard deviation; 12) Gram; 13) Nanogram

Table 2. Frequencies of gender, type of dialysis and duration from starting dialysis per study groups

Variable	Anxiety disorder N (%)	No anxiety disorder N (%)	P value [1]	Depression disorder N (%)	No depression disorder N (%)	P value
Girls (n=18)	17 (94.4)	1 (5.6)	0.07	12 (66.7)	6 (33.3)	0.91[2]
Boys (n=22)	16 (72.7)	6 (27.3)		15 (68.2)	7 (31.8)	
HD[3] patients (n=18)	16 (88.9)	2 (11.1)	0.33	14 (77.8)	4 (22.2)	0.20[1]
PD[4]patients (n=22)	17 (77.3)	5 (22.7)		13 (59.1)	9 (40.9)	
Duration from starting dialysis ≤ one year (n=14)	13 (92.9)	1 (7.1)	0.20	10 (71.4)	4 (28.6)	0.69[1]
Duration from starting dialysis > one year (n=26)	20 (76.9)	6 (23.1)		17 (65.4)	9 (34.6)	
Total patients (%)	33(100)	7 (100)	----------	27(100)	13(100)	----------

1) Fisher exact test; 2) Chi square test; 3) Hemodialysis; 4) peritoneal dialysis

Table 3. Serologic and anthropometric parameters in patients with and without mood disorders

Variable	Anxiety disorder (n=33)	No anxiety disorder (n=7)	P value	Depression disorder (n=27)	No depression disorder (n=13)	P value[1]
Serum Hb[2](mg[3]/dl[4])	11.48±1.62	10.41±1.3	0.11	11.42±1.59	11.02±1.66	0.46
Serum Urea(mg/dl)	131.72±38.54	131.02±59.95	0.96	128.48±34.31	138.09±56.04	0.50
Serum albumin(mg/dl)	4.2±0.3	4.14±0.29	0.65	4.18±0.29	4.2±0.33	0.88
Serum Zinc(ng [5]/dl)	94.75±18.22	90.71±21.98	0.60	91.77±17.19	98.76±21.4	0.27
Serum Copper(ng/dl)	88.18±12.33	89.14±18.2	0.86	87.18±11.35	90.76±16.83	0.43
Serum Selenium (µg[6] /l[7])	93.44±7.28	91.68±8.91	0.57	92.23±7.22	95.01±7.98	0.27
Serum Vitamin E(µg/l)	14.72±3.54	13.3±4.89	0.37	15.41±3.16	12.53±4.33	**0.02**
Z score of length for age	-0.66 ±1.8	-0.64±1.8	0.98	-0.69±1.69	-0.58±2.1	0.86

1) Independent sample t test ; 2) Hemoglobin ;3) Milligram; 4) Deciliter ; 5) Nano gram ; 6) Micro gram ; 7)Liter

Table 4. Serologic and anthropometric parameters in patients with and without mood disorders

Variable	Anxiety disorder Median (IQRs)[2]	No anxiety disorder Median (IQRs)	P value	Depression disorder) Median (IQRs)	No depression disorder Median (IQRs)	P value[1]
Age (year)	11(8-14)	8(7-12)	0.26	11 (8, 15)	8 (6.75, 12)	0.18
Z score of Weight for age	0.1 (-2.3, 1.1)	0.05 -1.6,0.89)	0.86	-0.68 (-2.3, 1)	0.7 (-1.65, 1.4)	0.40
Serum Iron (µg [3]/dl [4])	58 (46,73)	52(45,114)	0.86	58 (45, 75)	56 (46.5, 84)	0.93
Serum Vitamin C (mg [5]/L[6])	5.3 (4,7.8)	5.2 (4.5, 5.5)	0.75	6.2 (4.3,9.2)	5 (4.1,5.45)	0.17
Serum Manganese (µg/L)	5.6 (4.05, 8.3)	6.8 (4.3, 11.5)	0.42	5.6 (4, 7.9)	7 (4.6, 11.75)	0.19
Duration from starting dialysi (yr)	2 (1,4)	4 (3-4)	0.27	2 (1-4)	3 (1,4)	0.86
Total cases (%)	33(100)	7 (100)	----- ----	27 (100)	13 (100)	----- ------

1) Mann-Whitney U test; 2) Interquartile ranges; 3) Microgram; 4) Deciliter; 5) Milligram; 6) Liter

Table 5. Comparison of Selenium and Copper deficiency in patients with and without mood disorders

Variable	Selenium deficient (<90 µg /l); N (%)	Selenium Sufficient (≥90 µg); N (%)	P value	Copper deficient (<80 ng/dl); N (%)	Copper sufficient (≥80 ng/dl); N (%)	P value [1]
Girls (n=18)	5 (27.8)	13 (72.2)	0.56 [1]	3 (16.7)	15 (83.3)	0.78
Boys(n= 22)	8 (36.4)	1 (63.6)		3 (13.6)	19 (86.4)	
HD[2] patients (n=18)	7 (38.9)	11 (61.1)	0.43[3]	2 (11.1)	16 (88.9)	0.53
PD[4] patients (n=22)	6 (27.3)	16 (72.7)		4 (18.2)	18 (81.8)	
Duration from starting dialysis ≤ one year (n=14)	6 (42.8)	8 (57.2)	0.30 [3]	1 (7.1)	13 (92.9)	0.30
Duration from starting dialysis > one year (n=26)	7 (26.9)	19 (73.1)		5 (19.2)	21 (80.8)	
Total cases	13	27		6	34	

1) Fisher exact test; 2) Hemodialysis; 3) Chi square test; 4) Peritoneal dialysis;

Discussion

In a cross-sectional study, 40 children undergoing dialysis were studied to determine the prevalence of depression and anxiety disorders as well as their relationship with serum levels of vitamin C, vitamin E, zinc, selenium, copper, and manganese. The role of gender, age, duration from the onset of dialysis, and serum levels of hemoglobin, BUN, iron (as parameters potentially affecting central nervous system function), and albumin (as a nutritional marker) was considered in the evaluation. Anxiety and depression disorders were prevalent in our cases (82.5% and 67.5%, respectively). We did not find any remarkable relationship between the aforementioned factors and depression or anxiety disorders, except that vitamin E level was significantly higher in patients with depression than in those without depression

Shih et al. have reported that in patients with CKD, serum levels of zinc substantially diminished with the progression of disease [17]. Our series included patients with CKD stage V. As our patients were receiving multivitamin-mineral supplements containing zinc salts, we did not find zinc deficiency. Maha et al. evaluated the association between trace element deficiency and depression in dialysis patients and compared the data with the control group **(22)**. They found a significant correlation between zinc deficiency and depression. Ekramzadeh et al. compared the frequency of depression disorders between dialysis and control groups **(23)**. The Beck Depression Inventory questionnaire is used to diagnose depression. We used the CDI and the DASS questionnaires. The frequency of depressive disorders in our cases was similar to that reported by Ekramzedeh (67.5% and 65%, respectively). Consistent with our findings, they found no relationship between selenium deficiency and depression.

Amira et al. **(24)** reported a higher frequency of depression in CKD stages III-V than the control group (23.7% versus 2 %; P< 0.001), respectively. In addition, the frequency of depression disorders in CKD patients on dialysis (34.5%) was higher than those in pre-dialysis (13.3%) (P=0.01). Selenium deficiency is suggested to be the most prominent diet-related factor associated with depression **(14)**. Depression has been reported as a prevalent psychological problem in adult HD patients (76%) **(25)**. In a study by Roozbeh et al (25).a significant lower level of zinc was reported in depressed patients compared to those without depression (67.46 ±29.7 versus 85.26±40.05). We did not find any striking difference in serum levels of zinc in patients with and without depression (91.77±17.19 versus 98.76±21.4 ng/dl). In our HD cases, anxiety disorders were more common than depressive disorders (88.9% compared to 77.8%, respectively).

Biomarkers were compared between depressed and non-depressed individuals in a meta-analysis of 34 studies with 5652 participants. They concluded that lower serum albumin levels were associated with both the incidence and severity of depression **(26)**. According to our data there was no significant difference in serum levels of albumin between depressed and non-depressed patients (4.18±0.29 versus 4.2±0.33, respectively; P=0.88). In our study, only two patients met the criteria for severe depression.

Although in our series, patients with depression had a notably higher serum level of vitamin E than non-depressed patients, the normal reference range of

serum vitamin E (11.9 - 30 µmol/L) was reported in all cases **(27)**. The anti-inflammatory and antioxidant pathways are involved in depression and anxiety **(28)**. Some studies suggest vitamin E may have antidepressant properties **(29-31)**. Maes et al. reported that the serum vitamin E level in patients with major depression is lower than in healthy ones **(32)**. Antioxidant defense mechanisms are reduced in CKD patients due to dietary restrictions and dialysis, which leads to the loss of vitamins C, vitamin E, and selenium **(33)**.

The majority of reports on vitamin E role in depression have focused on comparing dialysis patients with healthy controls. In addition, the included dialysis participants did not receive daily vitamin E supplementation. Because of the confirmed vitamin E role in reducing oxidative stress in dialysis patients, all of our patients received daily vitamin E (12.5-50 mg in combination with vitamin C, 15-60 mg, and zinc, 6.25 -25 mg). We found no explanation for the significantly higher serum vitamin E level in depressed patients vs. cases without depression. No finding has been reported before.

The range of 5.5-17 µg/mL in adults is considered as normal. In children, it is 3-18.4 µg/ml. Although the major hazardous complications of increased vitamin E levels include bleeding, others have been mentioned including emotional disorder **(34)**. In our series, the serum vitamin E levels were in the upper limits of normal (18 µg/ml) or high (> 18 µg/ml) in seven cases (25.9%) with depression and high in three cases without depression (23%). Searching the literature, we did not find an article on the relationship between vitamin E levels and depression. Most papers have investigated the relationship between vitamin E deficiency and mood disorders. We do not know why 17.5 % of total patients (n=7) had symptoms of depression despite serum vitamin E levels ≥ 18 µg/ml.

Diminished micronutrient intake is common in peritoneal dialysis patients. According to Martín-del-Campo et al **(35)**, 50% of PD patients had a low intake of iron, zinc, B6, C, niacin, and folic acid in their diet. All of our cases including PD and HD patients routinely received Nephrotonic or Nephrovite supplements specific for dialysis patients, which contain zinc, folic acid, vitamin B6, C, niacin and vitamin E. Adding these supplements to the therapeutic regimen helped prevent vitamin E and zinc deficiencies in our cases

A recent review study evaluated micronutrient status during renal replacement therapy (RRT) **(36)**. Among trace elements, a negative balance was found for copper and selenium. Smaller water-soluble vitamins were found in the effluent, but larger lipid-soluble vitamins were not. Among 35 publications reviewed, three compared the impact of RRT modality. They found that the type of modality affects the total losses. Three papers reported a significant loss of copper in the dialysate on PD cases. Changes in blood trace elements levels were evaluated in eight studies, most reported lowered levels of copper, selenium, and zinc over time.

Most studies about trace elements status in CKD have focused on patients receiving HD. Such types of studies in PD cases are limited. In addition, few studies have assessed trace element excretion in the PD population. Xiang et al **(37)** measured the dialysate and urine concentration of copper, zinc, and selenium in healthy and continuous ambulatory peritoneal dialysis (CAPD) subjects. They found that CAPD patients lost more Cu than healthy subjects did. In addition, nonanuic CAPD patients may develop a deficiency of some trace elements while anuric patients are at risk of arsenic accumulation.

Limitations

The main limitation of present study was its small sample size. Meanwhile, the absence of a healthy control group may be considered another limitation. As many studies are available, in the literature with a case-control design that compares serum levels of trace elements, vitamin E and C Levels, and frequency of anxiety and depression disorders between dialysis and healthy groups.

The main positive point of the current study was that the dialysis population enrolled in the study and the association between serum trace elements level, vitamin E, and C was compared between patients with and without mood disorders (anxiety and depression). Few studies have been conducted on anxiety disorders in dialysis patients; however, in our investigation, both anxiety and depression disorders were assessed separately.

Conclusion

We found that both anxiety and depression disorders are prevalent in the pediatric dialysis population. In addition, selenium and copper deficiencies were frequent. In contrast to adults on dialysis, anxiety disorders were more frequent than depression in our cases. Serum levels of zinc, selenium, copper, manganese, and vitamin C were not associated with depression or anxiety disorders. A higher serum level of vitamin E was an unreported finding in our series. Further investigation is required to answer this question: ‘Does the significantly higher serum levels of vitamin E in depressed than in non-depressed patients (which did not exceed the normal range) have any role in the pathogenesis of depression?’.

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Authors’ Contribution

M.N, E.B, P.H: conception or design, E.B, M.N, L.K: acquisition, analysis, M.N, E.B, L.K, P.H: drafting the work. E.B, M.N, L.K, P.H: final approval.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethics Approval and consent to participate

The Ethics Committee of Mashhad University of Medical Sciences approved the study protocol (ethic code: IR. MUMS. fm. REC.1396.494).

References

1. Amanullah F, Malik AA, Zaidi Z. Chronic kidney disease causes and outcomes in children: Perspective from a LMIC setting. PloS one. 2022;17(6):e0269632. https://doi.org/10.1371/journal.pone.0269632 PMid:35675292 PMCid:PMC9176774

2. Kogon AJ, Vander Stoep A, Weiss NS, Smith J, Flynn JT, McCauley E. Depression and its associated factors in pediatric chronic kidney disease. Pediatr Nephrol. 2013;28(9):1855-61. https://doi.org/10.1007/s00467-013-2497-5 PMid:23700174 PMCid:PMC3897296

3.Moreira JM, Bouissou Morais Soares CM, Teixeira AL, Simões e Silva AC, Kummer AM. Anxiety, depression, resilience, and quality of life in children and adolescents with pre-dialysis chronic kidney disease. Pediatr Nephrol. 2015;30(12):2153-62. https://doi.org/10.1007/s00467-015-3159-6 PMid:26210984

4.Feroze U, Martin D, Reinapatton A, Kalantarzadeh K, Kopple JD. Mental health, depression, and anxiety in patients on maintenance dialysis. 2010.

5. Makoff R. Water-soluble vitamin status in patients with renal disease treated with hemodialysis or peritoneal dialysis. J Renal Nutr. 1991;1(2):56-73. https://doi.org/10.1016/S1051-2276(12)80195-6

6. Shanmugam L, Green SR, Radhakrishnan H, Kadavanu TM, Ramachandrappa A, Tiwari SR, et al. Trace elements in chronic haemodialysis patients and healthy individuals-A comparative study. J Clin Diag Res.2016;10(10):OC14.

7.Sajjadi SS, Foshati S, Haddadian-Khouzani S, Rouhani MH. The role of selenium in depression: a systematic review and meta-analysis of human observational and interventional studies. Sci Rep. 2022;12(1):1-13. https://doi.org/10.1038/s41598-022-05078-1 PMid:35058530 PMCid:PMC8776795

8.Lee SH, Huang JW, Hung KY, Leu LJ, Kan YT, Yang CS, et al. Trace Metals' abnormalities in hemodialysis patients: relationship with medications. Artif Organs. 2000;24(11):841-4. https://doi.org/10.1046/j.1525-1594.2000.06352.x PMid:11119069

9.Vanholder R, Cornelis R, Dhondt A, Lameire N. The role of trace elements in uraemic toxicity. Nephrol Dialys Transplant. 2002;17(suppl_2):2-8. https://doi.org/10.1093/ndt/17.suppl_2.2 PMid:11904350

10. Chen J, Berry MJ. Selenium and selenoproteins in the brain and brain diseases. J Neurochem. 2003;86(1):1-12. https://doi.org/10.1046/j.1471-4159.2003.01854.x PMid:12807419

11. Rederstorff M, Krol A, Lescure A. Understanding the importance of selenium and selenoproteins in muscle function. Cell Molec Life Sci. 2006;63(1):52-9. https://doi.org/10.1007/s00018-005-5313-y PMid:16314926 PMCid:PMC2792354

12. Cukor D, Coplan J, Brown C, Friedman S, Newville H, Safier M, et al. Anxiety disorders in adults treated by hemodialysis: a single-center study. Am J Kidney Dis. 2008;52(1):128-36. https://doi.org/10.1053/j.ajkd.2008.02.300 PMid:18440682

13. Mosleh H, Alenezi M, Alsani A, Fairaq G, Bedaiwi R. Prevalence and factors of anxiety and depression in chronic kidney disease patients undergoing hemodialysis: a cross-sectional single-center study in Saudi Arabia. Cureus. 2020;12(1). https://doi.org/10.7759/cureus.6668 PMid:31976185 PMCid:PMC6968827

14. Czaderny K. Risk factors for depression. New evidence on selenium deficiency and depressive disorders. Psychiatr Pol. 2020;54(6):1109-21.

https://doi.org/10.12740/PP/112967
PMid:33740799

15.Juma R, Onyango A, Ouma C. The Role of Trace Minerals in Depression: A Review of Selenium Iron and Copper. 2020.

16.Hou Y, Li X, Yang L, Liu C, Wu H, Xu Y, et al. Factors associated with depression and anxiety in patients with end-stage renal disease receiving maintenance hemodialysis. Int Urol Nephrol. 2014;46(8):1645-9.
https://doi.org/10.1007/s11255-014-0685-2
PMid:24619584

17.Shih CT, Shiu Y-L, Chen C-A, Lin H-Y, Huang Y-L, Lin C-C. Changes in levels of copper, iron, zinc, and selenium in patients at different stages of chronic kidney disease. Genom Med Biomarker Health Sci. 2012;4(4):128-30.
https://doi.org/10.1016/j.gmbhs.2013.03.001

18. Schwotzer N, Kanemitsu M , Kissling S , Darioli R , Benghezal M , Rezzi S .et al .Water-soluble vitamin levels and supplementation in chronic online hemodiafiltration patients. Kidney Int Rep. 2020 ; 12;5(12):2160-2167.
https://doi.org/10.1016/j.ekir.2020.09.009
PMid:33305108 PMCid:PMC7710883

19. Clase CM, Ki V, Holden RM . Water-soluble vitamins in people with low glomerular filtration rate or on dialysis:a review.Semin Dial. 2013 ;26(5):546-67.
https://doi.org/10.1111/sdi.12099
PMid:23859229 PMCid:PMC4285924

20. Escobedo-Monge MF, Ayala-Macedo G, Sakihara G, Peralta S, Almaraz-Gómez A, Barrado E, et al . Effects of zinc supplementation on nutritional status in children with chronic kidney disease: a randomized trial. Nutrients .2019 ; 5;11(11):2671.
https://doi.org/10.3390/nu11112671
PMid:31694220 PMCid:PMC6893698

21.Galli F, Bonomini M, Bartolini D, Zatini L, Reboldi G, Marcantonini G, et al . Vitamin E (alpha-tocopherol) metabolism and nutrition in chronic kidney disease..Antioxidants (Basel). 2022; 18;11 (5):989.
https://doi.org/10.3390/antiox11050989
PMid:35624853 PMCid:PMC9137556

22.Hassan MA, Wahab W, Elshafie T, Eid KA. Serum level of zinc and copper as predictors of severity of depression in chronic hemodialysis patients. World J Med Sci. 2014;10(3):240-9.

23. Ekramzadeh M, Mazloom Z, Sagheb M. Association of depression with selenium deficiency and nutritional markers in the patients with end-stage renal disease on hemodialysis. J Renal Nutr. 2015;25(4):381-7.
https://doi.org/10.1053/j.jrn.2014.12.005
PMid:25680525

24. Amira O. Prevalence of symptoms of depression among patients with chronic kidney disease. Nigerian J Clin Pract. 2011;14(4):460-3.
https://doi.org/10.4103/1119-3077.91756
PMid:22248950

25. Roozbeh J, Sharifian M, Ghanizadeh A, Sahraian A, Sagheb MM, Shabani S, et al. Association of zinc deficiency and depression in the patients with end-stage renal disease on hemodialysis. J Renal Nutr. 2011;21(2):184-7.
https://doi.org/10.1053/j.jrn.2010.05.015
PMid:21093288

26. Gregg LP, Carmody T, Le D, Martins G, Trivedi M, Hedayati SS. A systematic review and meta-analysis of depression and protein-energy wasting in kidney disease. Kidney Int Rep. 2020;5(3):318-30.
https://doi.org/10.1016/j.ekir.2019.12.009
PMid:32154453 PMCid:PMC7056860

27.Tiemeier H, Hofman A, Kiliaan AJ, Meijer J, Breteler MM. Vitamin E and depressive symptoms are not related. The Rotterdam Study. J Affect Disord. 2002;72(1):79-83.
https://doi.org/10.1016/S0165-0327(01)00427-X
PMid:12204320

28.Lee ARYB, Tariq A, Lau G, Tok NWK, Tam WWS, Ho CSH. Vitamin E, Alpha-Tocopherol, and its effects on depression and anxiety: A systematic review and meta-analysis. Nutrients. 2022;14(3):656.
https://doi.org/10.3390/nu14030656
PMid:35277015 PMCid:PMC8840247

29. Lobato KR, Cardoso CC, Binfaré RW, Budni J, Wagner CL, Brocardo PS, et al. α-Tocopherol administration produces an antidepressant-like effect in predictive animal models of depression. Behav Brain Res. 2010;209(2):249-59.
https://doi.org/10.1016/j.bbr.2010.02.002
PMid:20144659

30.Manosso LM, Neis VB, Moretti M, Daufenbach JF, Freitas AE, Colla AR, et al. Antidepressant-like effect of α-tocopherol in a mouse model of depressive-like behavior induced by TNF-α. Prog Neuro-Psychopharmacol Biol Psychiatr. 2013;46:48-57. https://doi.org/10.1016/j.pnpbp.2013.06.012 PMid:23816813

31.Huang X, Wu H, Jiang R, Sun G, Shen J, Ma M, et al. The antidepressant effects of α-tocopherol are related to the activation of autophagy via the AMPK/mTOR pathway. Europ J Pharmacol. 2018;833:1-7. https://doi.org/10.1016/j.ejphar.2018.05.020 PMid:29782858

32.Maes M, De Vos N, Pioli R, Demedts P, Wauters A, Neels H, et al. Lower serum vitamin E concentrations in major depression: Another marker of lowered antioxidant defenses in that illness. J Affect Disord. 2000;58(3):241-6. https://doi.org/10.1016/S0165-0327(99)00121-4 PMid:10802134

33. Rapa SF, Di Iorio BR, Campiglia P, Heidland A, Marzocco S. Inflammation and oxidative stress in chronic kidney disease-the potential therapeutic role of minerals, vitamins, and plant-derived metabolites. Int J Molec Sci. 2019;21(1):263. https://doi.org/10.3390/ijms21010263 PMid:31906008 PMCid:PMC6981831

34. Kristen N. Owen; Olga Dewald. Vitamin E Toxicity . StatPearls [Internet]. Avilable at : https://www.ncbi.nlm.nih.gov › books › NBK564373.

35. Martín-del-Campo F, Batis-Ruvalcaba C, González-Espinoza L , Rojas-Campos E , Angel JR , Ruiz N , et al .Dietary micronutrient intake in peritoneal dialysis patients: relationship with nutrition and inflammation status. Perit Dial Int. 2012 ;32(2):183-91. https://doi.org/10.3747/pdi.2010.00245 PMid:21804135 PMCid:PMC3525406

36 . Bergera MM, Bromanb M , Fornic L, Ostermannd M , Waelee ED , Wischmeyer PE. Nutrients and micronutrients at risk during renal replacement therapy: a scoping review. Curr Opin Crit Care. 2021; 27(4): 367-377. https://doi.org/10.1097/MCC.0000000000000851 PMid:34039873 PMCid:PMC8270509

37. Xiang S, Yao Y , Wan Y, Liang W , Meng R, Jin Q, et al . Comparative study on trace element excretions between nonanuric and anuric patients undergoingcontinuous ambulatory peritoneal dialy. Nutrients . 2016; 8: 826. https://doi.org/10.3390/nu8120826 PMid:27999390 PMCid:PMC5188479

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