



# Prevalence of Electrolyte Impairments Among Outpatient Elderly Subjects

## Ayaktan Takip Edilen Yaşlı Bireylerde Elektrolit İmbalanslarının Prevalansı

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### ABSTRACT

**Objective:** To determine the prevalence of different electrolyte imbalances in a cohort of elderly subjects aged  $\geq 65$  years, and evaluate associations between each electrolyte imbalance and functional dependence.

**Methods:** We reviewed medical records of consecutive outpatient elderly subjects. Frequency of hyponatremia (serum sodium of  $<136$  mmol/L), hypernatremia (serum sodium of  $>145$  mmol/L), hypokalemia (serum potassium of  $<3.5$  mEq/L), hyperkalemia (serum potassium of  $>5.3$  mEq/L), hypocalcemia (serum calcium of  $<8.5$  mg/dL), hypercalcemia (serum calcium of  $>10.5$  g/dL), hypophosphatemia (serum phosphorus of  $<2.5$  mg/dL), hyperphosphatemia (serum phosphorus of  $>4.5$  mg/dL), hypomagnesemia (serum magnesium of  $<1.6$  mg/dL), and hypermagnesemia (serum magnesium of  $>2.3$  mg/dL) were assessed. Associations between each electrolyte disorder and Barthel and Lawton-Brody activities of daily living (BADL and IADL) were analyzed.

**Results:** Among the 464 subjects, hyponatremia (11.2%) hypomagnesemia (9.1%) and hypermagnesemia (8.8%) were the most common disorders. Patients with one electrolyte imbalance constituted 30.2% (140 patients) of the cohort, while 44 (9.5%) had two, and 7 (1.5%) patients had  $\geq 2$  electrolyte imbalances, concurrently. Calcium, phosphorus, and magnesium disorders were more common among subjects who were 80 years of age or more, compared to those aged 65-79 years, while the frequency of potassium disorders was lower in the former group. Hyponatremia

### ÖZ

**Amaç:** Yaşlı bireylerden ( $\geq 65$  yaş) oluşan bir kohortta farklı elektrolit bozukluklarının sıklığının belirlenmesi ve her bir bozukluğun fonksiyonel bağımlılık ile ilişkisinin değerlendirilmesi amaçlanmıştır.

**Yöntemler:** Ardışık olarak ayaktan takip edilen yaşlı bireylerin tıbbi kayıtları geriye dönük incelendi. Hiponatremi (serum sodyum  $<136$  mmol/L), hipernatremi (serum sodyum  $>145$  mmol/L), hipokalemi (serum potasyum  $<3,5$  mEq/L), hiperkalemi (serum potasyum  $>5,3$  mEq/L), hipokalsemi (serum kalsiyum  $<8,5$  mg/dL), hiperkalsemi (serum kalsiyum  $>10,5$  g/dL), hipofosfatemi (serum fosfor  $<2,5$  mg/dL), hiperfosfatemi (serum fosfor  $>4,5$  mg/dL), hipomagnezemi (serum magnezyum  $<1,6$  mg/dL) ve hipermagezemi (serum magnezyum  $>2,3$  mg/dL) sıklıkları değerlendirildi. Her bir elektrolit bozukluğunun Barthel ve Lawton-Brody günlük yaşam aktiviteleri skorları (BADL and IADL) ile ilişkileri analiz edildi.

**Bulgular:** Dahil edilen 464 bireyde, hiponatremi (%11,2) hipomagnezemi (%9,1) ve hipermagezemi (%8,8) en sık bozukluklar olarak dikkati çekti. Bir elektrolit bozukluğu olan hastalar kohortun %30,2'sini (140 hasta) oluştururken, 44 (%9,5) hastada iki ve 7 (%1,5) hastada 2 ve üzeri elektrolit imbalansı saptandı. Kalsiyum, fosfor, ve magnezyum bozuklukları 80 yaş ve üzeri bireylerde 65-79 yaş aralığı bireylere kıyasla daha sık görülürken, potasyum bozuklukları ilk grupta daha az sıklıkta idi. Hiponatremi ve hipokalseminin BADL ve IADL skorlarına göre fonksiyonel bağımlılıkla anlamlı derecede birlikte görüldüğü

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and hypocalcemia were associated with functional dependence based on BADL and IADL scores. Patients with multiple electrolyte abnormalities had a higher risk of functional dependence.

**Conclusion:** Hypomagnesemia was as common as hyponatremia, especially among patients with an age of 80 years or more. Hyponatremia and hypocalcemia appeared to be associated with functional dependence. The higher number of electrolyte abnormality the higher risk of functional dependence. Our results should be confirmed by studies with larger sample sizes.

**Keywords:** Elderly, electrolyte, magnesium

saptandı. Eş zamanda çok sayıda elektrolit bozukluğu olan kişilerin fonksiyonel bağımlılık riskinin arttığı gözlemlendi.

**Sonuç:** Hipomagnezemi hiponatremi kadar sık olup, özellikle 80 yaş ve üzeri bireylerde daha sıktır. Hiponatremi ve hipokalsemi fonksiyonel bağımlılık ile ilişkili görünmektedir. Elektrolit bozukluklarının sayısı arttıkça fonksiyonel bağımlılık riski de artmaktadır. Sonuçlarımız daha büyük çalışmalarla doğrulanmalıdır.

**Anahtar Sözcükler:** Yaşlı, elektrolit, magnezyum

## Introduction

Electrolyte imbalances are common in the elderly and prevalences are increased by age (1,2). Elderly patients may be more prone to develop electrolyte abnormalities due to physiological changes of the kidney (3). Electrolyte abnormalities may be associated with a longer hospital stay or mortality among subjects who are admitted to hospital (4). Many previous studies have shown that hyponatremia is the most common electrolyte disorder in the elderly (3). Although the current literature suggests that hyponatremia is the most prevailing electrolyte abnormality, the prevalence of various electrolyte abnormalities has rarely been studied in the same cohort. Liamis et al. (1) recruited subjects who were aged 55 years or more from the general population and assessed electrolyte abnormalities and risk factors for these disorders. However, they mainly focused on hyponatremia, hypernatremia, hypokalemia, hyperkalemia, and hypomagnesemia. Another study investigated the frequency of electrolyte disorders (4), but the age cut-off for inclusion criteria was 18 years or older. Moreover, the study sample comprised of subjects who were admitted to emergency department. Several electrolyte disorders in these studies were associated with mortality, longer hospital stay and/or readmission.

Despite the wide range of studies, no study has evaluated frequency of all electrolyte abnormalities in an elderly outpatient setting. In this paper, we aimed to evaluate the frequency of sodium, potassium, calcium, phosphorus, and magnesium abnormalities in serum of elderly subjects who were admitted to a single outpatient geriatric clinic in Turkey.

## Methods

This study was approved by the Institutional Review Board of our institution (IRB code: 54022451-050.05.04-; 25.08.2020). Patients who presented to outpatient geriatric clinics between July 2016 through April 2020 were included. All participants were  $\geq 65$  years of age. Their demographic data were recruited from patient files.

The definitions for each electrolyte abnormality were as follows:

- Hyponatremia: serum sodium concentration of  $<136$  mmol/L (5).

- Hypernatremia: serum sodium concentration of  $>145$  mmol/L (6).
- Hypokalemia: serum potassium concentration of  $<3.5$  mmol/L (7).
- Hyperkalemia: serum potassium concentration of  $>5.3$  mmol/L (7).
- Hypocalcemia: serum calcium (total) concentration of  $<8.5$  mg/dL (8).
- Hypercalcemia: serum calcium (total) concentration of  $>10.5$  mg/dL (8).
- Hypophosphatemia: serum phosphorus concentration of  $<2.5$  mg/dL (9).
- Hyperphosphatemia: serum phosphorus concentration of  $>4.5$  mg/dL (9).
- Hypomagnesemia: serum magnesium concentration of  $<1.6$  mg/dL (10).
- Hypermagnesemia: serum magnesium concentration of  $>2.3$  mg/dL (9).

Sodium and calcium concentrations were corrected for blood glucose and serum albumin levels. All of the measurements were performed as a part of the comprehensive geriatric assessment.

Associations between each of electrolyte imbalance with basic activities of daily living (BADL) and instrumental activities of daily living (IADL) were assessed. The BADL is a scale that includes 10 questions about the ability to provide self-care, use toilet, get dressed, eat, urinary and fecal continence, use the stairs, move from bed to chair, and mobility (11). Scoring is as follows:

- 0-20 points, completely dependent
- 21-61 points, severely dependent
- 62-90 points, moderately dependent
- 91-99 points, mildly dependent
- 100 points, independent

The Lawton-Brody IADL index has been proposed as a means to determine the instrumental activities of daily living of

subjects, which includes 8 questions about telephone usage, preparing meals, shopping, doing daily house works, laundry, transportation, taking pills, and money management (12).

The scoring is as follows:

- 0-8 points, dependent
- 9-16 points, semi-dependent
- 17-24 points, independent

The Mini Nutritional Assessment (MNA) was used for nutritional evaluation. A total MNA score of <17 was accepted as malnutrition (13).

### Statistical Analysis

Quantitative variables were expressed as median with the interquartile range (25-75%). Qualitative variables were expressed as proportions. Groups were compared for means using the Mann-Whitney U test or the Kruskal-Wallis test, as appropriate. Chi-squared tests were used for comparisons between proportions. Associations between each electrolyte abnormality and ADL indexes were assessed by logistic regression analysis. Results were expressed as odds ratios and 95% confidence intervals for logistic regression. Statistical analysis was performed using SPSS 22.0 version (IBM SPSS, Chicago, IL). A P value of 0.05 or lower was considered to be statistically significant.

### Results

Among the 1,802 consecutively evaluated elderly subjects, 1,310 lacking electrolyte measurements and 28 with no ADL evaluation were excluded. Finally, the cohort included 464 patients. The median age was 78 (72-83) years and 321 (69.2%) were women. Hypertension (HT), diabetes mellitus (DM), and chronic kidney disease (CKD) were present in 69%, 36%, and 39% of the subjects, respectively. Overall, 195 (41.2%) patients had at least one electrolyte imbalance. The frequency of each disorder was as follows: hyponatremia, 11.2%; hypernatremia, 1.7%; hypokalemia, 1.7%; hyperkalemia, 6.7%; hypocalcemia, 4.7%; hypercalcemia, 2.6%; hypophosphatemia, 5.0%; hyperphosphatemia, 2.6%; hypomagnesemia, 9.1%; and hypermagnesemia, 8.8%.

#### Hyponatremia

A total of 52 patients (11.2%) had hyponatremia. The median sodium level was 140 (138-142) mmol/L. Median glomerular filtration rate among patients with hyponatremia was lower than patients with normonatremia, but this was not statistically significant (median 63 versus 69 mL/min/1.73 m<sup>2</sup>, p=0.064). Median BADL and IADL scores were 76 versus 85 and 8 versus 14 among patients with hyponatremia and normonatremia, respectively (p values 0.001 and 0.016, respectively). The median age and sex distribution were comparable between hyponatremia and normonatremia groups.

For the BADL, dependence was more commonly observed among patients with hyponatremia (p=0.005, Table 2). This

was also the case based on the IADL scores (p=0.027). The association between hyponatremia and the grade of dependency based on BADL remained significant in patients with an age of 80 years or older, while the significance was lost in patients with an age of 65 to 79 years. In the contrary, the association between hyponatremia and the grade of dependency based on the IADL was significant for patients with an age of 65 to 79 years, but not for those who were ≥80 years of age. Although more commonly seen in subjects with chronic kidney disease, and those who were exposed to thiazide diuretics and overall anti-hypertensives, we could not observe a significant association between hyponatremia and any of these factors.

#### Hypernatremia

Only 8 (1.7%) patients had hypernatremia by definition. All of the patients had a serum sodium of 146 mmol/L. In this group with a quite low sample size, we could not find a significant association between age, sex, drug exposures, and BADL/IADL scores with hypernatremia.

#### Hypokalemia

Only 8 (1.7%) patients had hypokalemia, with a median potassium level of 3.2 (2.9-3.4) mEq/L. Similar to the hypernatremia group, we could not find a significant association between age, sex, drug exposures, and BADL/IADL scores and hypernatremia. None of the 8 patients with hypokalemia had chronic kidney disease.

#### Hyperkalemia

Thirty-one (6.7%) patients had hyperkalemia, with a median serum potassium of 5.6 (5.5-5.9) mEq/L. The median estimated glomerular filtration rate (eGFR) of patients with hyperkalemia was significantly lower in comparison to patients with normokalemia (53 vs 69 mL/min/1.73 m<sup>2</sup>, p<0.001). Age and sex distribution were comparable across groups. Patients with hyperkalemia were more likely to have dependence based on BADL and IADL total scores, and there was trend toward significance for each comparison (p=0.059 for both comparisons). Significances were lost when hyperkalemia versus normokalemia were compared for different categorizations of BADL and IADL indexes.

#### Hypocalcemia

Twenty-two (4.7%) patients had hypocalcemia, with a median serum total calcium of 8.3 (8.1-8.4) mg/dL. Similar to patients with hyperkalemia, patients with hypocalcemia had a lower median eGFR compared to patients with normal serum calcium levels (48 vs 68 mL/min/1.73 m<sup>2</sup>, p=0.035). In addition to a lower median eGFR value, patients with hypocalcemia had a higher median serum magnesium level (2.1 versus 1.9 mg/dL, p=0.04). Age and sex distributions were comparable, but patients with hypocalcemia were significantly more dependent based on BADL and IADL scores (p values 0.004 and <0.001, respectively). This was also significant when BADL and IADL categorizations were assessed for associations with hypocalcemia.

### Hypercalcemia

Of the 12 (2.6%) patients with hypercalcemia, the median serum calcium level was 10.9 (10.7-10.9) mg/dL. The highest serum calcium was 11.0 mg/dL. No significant association was found in terms of age, sex, drug exposures, kidney functions, and BADL/IADL scores in comparisons between hypercalcemia versus normocalcemia groups.

### Hypophosphatemia

Of the 23 patients with hypophosphatemia, the median serum phosphate was 2.3 (2.1-2.4) mg/dL. DM was recorded in 37% of patients with normophosphatemia versus 13.6% of patients with hypophosphatemia. Similarly, CKD was also more common in the latter group, although not significant. Patients with normophosphatemia were more likely to be dependent based on BADL scores, but not IADL scores.

### Hyperphosphatemia

Median phosphorus level of 12 subjects with hyperphosphatemia was 5.0 (4.7-5.3) mg/dL. According to IADL scores, patients with hyperphosphatemia were more likely to be dependent (p=0.065).

**Table 1.** General characteristics of the total cohort.

Variable	
Age, years	78 (72-83)
Female sex	69.2%
Comorbidities	
Diabetes mellitus	36%
Hypertension	69%
Chronic kidney disease	39%
Heart failure	11%
Ischaemic heart disease	15%
Cerebrovascular disease	13%
Drug exposures	
Insulin	15%
ACEi/ARB	58%
Beta-blockers	24%
Loop diuretics	5%
Thiazides	48%
Spironolactone	2%
Polypharmacy	43%
Hemoglobin, g/dL	12.6 (11.4-13.8)
Serum creatinine, mg/dL	0.89 (0.75-1.15)
Glomerular filtration rate, ml/min/1.73 m <sup>2</sup>	68 (50-83)
Serum sodium, mmol/L	140 (138-142)
Serum potassium, mmol/L	4.4 (4.1-4.8)
Serum magnesium, mmol/L	2.0 (1.8-2.1)
Serum calcium, mmol/L	9.4 (9.1-9.8)
Serum phosphorus, mmol/L	3.3 (3.0-3.7)
Numerical variables are presented as median with the interquartile range (25-75%). ACEi/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker	

**Table 2.** Associations of electrolyte abnormalities with instrumental activities of daily living scores.

The Barthel BADL	HypoNa <sup>+</sup> versus NormoNa <sup>+</sup>		HyperNa <sup>+</sup> versus NormoNa <sup>+</sup>		HypoK <sup>+</sup> versus NormoK <sup>+</sup>		HyperK <sup>+</sup> versus NormoK <sup>+</sup>		HypoCa <sup>++</sup> versus NormoCa <sup>++</sup>		HyperCa <sup>++</sup> versus NormoCa <sup>++</sup>		HypoPO <sub>4</sub> versus NormoPO <sub>4</sub>		HyperPO <sub>4</sub> versus NormoPO <sub>4</sub>		HypoMg <sup>++</sup> versus NormoMg <sup>++</sup>		HyperMg <sup>++</sup> versus NormoMg <sup>++</sup>	
	p-value	0.005	0.454	0.879	0.424	<0.001	0.226	0.015	0.468	0.072	0.239	0.065	0.102	0.312						
Complete Dependence	11.5%/4.2%	0.0%/4.2%	0.0%/4.9%	6.5%/4.9%	27.3%/4.0%	0.0%/4.0%	0.0%/5.1%	8.3%/5.1%	2.4%/4.5%	12.2%/4.5%										
severe	25.0%/15.8%	0.0%/15.8%	25.0%/16.0%	22.6%/16.0%	27.3%/16.3%	8.3%/16.3%	8.3%/17.2%	8.3%/17.2%	31.0%/15.0%	17.1%/15.0%										
Dependence moderate	44.2%/44.1%	37.5%/44.1%	37.5%/43.5%	51.6%/43.5%	31.8%/43.7%	75.0%/43.7%	47.8%/44.1%	33.3%/44.1%	45.2%/44.9%	34.1%/44.9%										
Dependence	17.3%/17.3%	37.5%/17.3%	25.0%/17.9%	12.9%/17.9%	9.1%/18.1%	16.7%/18.1%	4.3%/18.4%	16.7%/18.4%	9.5%/18.6%	17.1%/18.6%										
Mild dependence	1.9%/18.6%	25.0%/18.6%	12.5%/17.6%	6.5%/17.6%	4.5%/17.9%	0.0%/17.9%	39.1%/15.2%	33.3%/15.2%	11.9%/17.1%	19.5%/17.1%										
Independence																				
p-value	0.005	0.454	0.879	0.424	<0.001	0.226	0.015	0.468	0.072	0.239	0.065	0.102	0.312							
The Lawton-Brody IADL																				
Dependent	53.8%/35.1%	0.0%/35.1%	37.5%/35.8%	48.4%/35.8%	59.1%/35.8%	25.0%/35.8%	30.4%/37.5%	16.7%/37.5%	47.6%/34.4%	46.3%/34.4%										
semi-dependent	19.2%/22.8%	50.0%/22.8%	12.5%/22.6%	29.0%/22.6%	18.2%/22.8%	33.3%/22.8%	21.7%/22.1%	50.0%/22.1%	26.2%/22.8%	19.5%/22.8%										
Independent	26.9%/42.1%	50.0%/42.1%	50.0%/41.6%	22.6%/41.6%	22.7%/41.4%	41.7%/41.4%	47.8%/40.3%	33.3%/40.3%	26.2%/42.8%	34.1%/42.8%										
p-value	0.027	0.066	0.781	0.112	0.079	0.623	0.741	0.065	0.102	0.312										

BADL: basic activities of daily living. IADL: instrumental activities daily of living.



**Table 3.** Frequency of electrolyte disorders according to different age groups.

Electrolyte impairment	Overall	65-79 years (n=269)	≥80 years (n=195)
Hyponatremia	52 (11.2%)	30 (11.2%)	22 (11.3%)
Hypernatremia	8 (1.7%)	5 (1.9%)	3 (1.5%)
Hypokalemia	8 (1.7%)	6 (2.2%)	2 (1.0%)
Hyperkalemia	31 (6.7%)	22 (8.2%)	9 (4.6%)
Hypocalcemia	22 (4.7%)	12 (4.5%)	10 (5.1%)
Hypercalcemia	12 (2.6%)	6 (2.2%)	6 (3.1%)
Hypophosphatemia	23 (5.0%)	10 (3.7%)	13 (6.7%)
Hyperphosphatemia	12 (2.6%)	5 (1.9%)	7 (3.6%)
Hypomagnesemia	42 (9.1%)	20 (7.5%)	22 (11.3%)
Hypermagnesemia	41 (8.8%)	21 (7.9%)	20 (10.3%)

### Hypomagnesemia

Forty-two patients had hypomagnesemia, and the median serum magnesium level was 1.5 (1.4-1.6) mg/dL. The frequency of hypomagnesemia was higher in patients with an age of >79 years compared to those with an age of 65 to 79 years. However, the severity of hypomagnesemia was similar. Hypomagnesemia was associated with dependency based on BADL and IADL scores ( $p=0.072$  and  $0.102$ , respectively). Patients with hypomagnesemia were older than patients with normomagnesemia, although not significant (median 81 vs 78,  $p=0.114$ ).

### Hypermagnesemia

Forty-one patients had hypermagnesemia, and they had a median serum magnesium of 2.4 (2.3-2.8) mg/dL. Similar to hypomagnesemia, hypermagnesemia was more common in ages over 79, but the severity of the disorder was comparable across age groups. The frequency of dependency was not significantly higher among subjects with hypermagnesemia.

### Interrelationships Between Electrolyte Abnormalities

There was no significant association between hypernatremia, hypokalemia, hypophosphatemia and other electrolyte disorders. The following associations were noted:

**Hyponatremia:** Patients with hyponatremia were more likely to have hypokalemia compared to patients without hyponatremia (15.4% versus 5.6%,  $p=0.008$ ). Similarly, hypocalcemia was also more commonly observed among patients with hyponatremia (11.5% versus 3.9%,  $p=0.014$ ). Patients with hyperkalemia more commonly had hyperphosphatemia compared to non-hyperkalemia ( $p<0.001$ ).

Hyperphosphatemia was present in 12.9% of patients with hyperkalemia while in 1.8% of those without hyperkalemia had hyperphosphatemia ( $p<0.001$ ).

**Hypocalcemia:** Hyperphosphatemia was more common in patients with hypocalcemia versus normocalcemia (9.1% vs 2.3%,  $p=0.049$ ). Hypermagnesemia was seen in 31.8% of patients with hypocalcemia versus 7.7% of patients with normocalcemia ( $p<0.001$ ).

**Hypercalcemia:** Twenty-five percent of patients with hypercalcemia had hypermagnesemia versus 8.4% of those without hypercalcemia had hypermagnesemia ( $p=0.080$ ).

**Hyperphosphatemia:** Of the patients with hyperphosphatemia, 25.0% had hypermagnesemia, while 8.2% of without hyperphosphatemia had hypermagnesemia ( $p=0.015$ ). Similarly, hyperkalemia (25.0% versus 6.0%,  $p<0.001$ ) was more common in patients with hyperphosphatemia.

**Hypomagnesemia:** Hyperkalemia was more common in patients with hypomagnesemia versus non-hypomagnesemia (14.3% versus 5.9%,  $p=0.005$ ). The majority of patients with hypomagnesemia plus hyperkalemia had DM (5 of 6 patients) versus 35.2% of the remaining ( $p=0.024$ ).

**Hypermagnesemia:** Of the 41 patients with hypermagnesemia 17% had hypocalcemia versus 3.5% of those without hypermagnesemia had hypocalcemia ( $p<0.001$ ). In the former group, 9.8% had hyperphosphatemia while 1.9% of the latter had hyperphosphatemia ( $p=0.015$ ).

### Associations with Age

Patients were divided into 2 groups in terms of age: 65-79 years and >79 years. The former group more commonly had DM (4.1% vs 28.0%,  $p=0.003$ ) and less frequently had CKD (32.0% vs 48.7%,  $p<0.001$ ). Calcium, phosphorus, and magnesium disorders were more common among subjects who were aged 80 years or more, compared to those aged 65-79 years, while frequency of potassium disorders were lower in the former group (Table 3).

### Associations with Comorbidities

The CKD comprised 91.7% of patients with hyperphosphatemia while 37.6% of patients without hyperphosphatemia had CKD ( $p<0.001$ ). Similarly, CKD was more common among patients with hyperkalemia versus non-hyperkalemia group (71% versus 36.7%,  $p<0.001$ ). None of the 8 patients with hypokalemia had CKD, in comparison, 39.7% of patients with non-hypokalemia had CKD ( $p=0.018$ ).

The DM was present in 70.7% of patients with hypomagnesemia and 32.4% of those without hypomagnesemia ( $p < 0.001$ ). This was in contrast to hypermagnesemia, 21.4% of whom had DM versus 36.9% in patients with non-hypermagnesemia ( $p = 0.111$ ). Similarly, patients with hypophosphatemia less frequently had DM than non-hypophosphatemic group (13.6% versus 36.9%,  $p = 0.026$ ). DM was more frequent among hyperkalemic subjects in comparison to non-hyperkalemia (61.3% versus 34.0%,  $p = 0.002$ ).

There was a reverse association between HT and hypophosphatemia. Half of these patients had HT while 69.6% of patients without hypophosphatemia had HT ( $p = 0.048$ ).

### Associations with Drug Exposures

Detailed descriptions of drug exposures were available in 449 subjects. A quarter of patients with hypophosphatemia had hyperpolypharmacy versus 3.3% of non-hypophosphatemics had hyperpolypharmacy, and there was trend towards significance ( $p = 0.057$ ). No other association was found with polypharmacy or hyperpolypharmacy and any electrolyte abnormality.

### Associations with Malnutrition

The MNA score was available in 212 subjects. Among patients with hypermagnesemia, 36.8% had malnutrition, and a similar percent were at risk of malnutrition, while 9.8% and 43.0% of patients without hypermagnesemia had malnutrition and were at risk of malnutrition, respectively ( $p = 0.002$ ).

### Multiple Electrolyte Abnormalities

Forty-four (9.5%) had two, and 7 (1.5%) had more than two concurrent electrolyte abnormalities. The most common disorders seen together were hyponatremia plus hypomagnesemia, and hyponatremia plus hyperkalemia each of which were concurrently seen in 8 (1.7%) patients. CKD was present in 35.2%, 40.7%, and 54.9% of patients with no electrolyte abnormality, single abnormality, and multiple abnormalities, respectively ( $p = 0.026$ ). Age, sex, and the frequency of DM were comparable among patients with no electrolyte abnormality, single abnormality, and multiple abnormalities. Median BADL score for no abnormality, single abnormality, and multiple abnormalities were 85 (70-95), 85 (65-95), and 80 (50-90), respectively ( $p = 0.014$ ). Median IADL score for same groups were 15 (6-20), 14 (5-20), and 10 (5-17), respectively ( $p = 0.08$ ).

### Discussion

Our study is the first to evaluate all electrolyte disorders in a single same cohort. The cohort included elderly subjects, who were more prone to develop such imbalances given the increased sensitivity to drug exposures and effects of comorbidities (3). We showed that magnesium disorders comprised the largest part of all abnormalities, particularly among subjects who were aged 80 years or more. Similarly, phosphate disorders were more common after the age of 80 years. In contrast, potassium disorders were less frequently observed in patients with an age of  $\geq 80$  years, in comparison to those aged 65 to 79 years. Others

reported dramatical increase in prevalences of hyponatremia and hyperkalemia with increasing age, but no such effect for hypernatremia and hypokalemia (14). Given that CKD was more common in the elderly, it is not unexpected to see an increase in the prevalence of hypermagnesemia with aging. However, it was worth to note that, hypomagnesemia was common after 80 years of age, despite the increased frequency of CKD and decreased frequency of DM. The majority of electrolyte imbalances were mild. However, sodium and calcium disorders were significantly associated with dependency based on BADL and IADL indexes. Furthermore, coexistent electrolyte abnormalities were more likely to be associated with dependency.

We recognized the limitation that at least some part of the association with dependency might come from comorbidities such as DM or CKD. Several abnormalities in our cohort were significantly associated with those comorbidities. Liamis et al. (1) studied the prevalence and risk factors of common electrolyte disorders in subjects with an age of 55 years or more who were recruited from the general population. The study mainly focused on hyponatremia, hypernatremia, hypokalemia, hyperkalemia, and hypomagnesemia. Fifteen percent of their cohort had at least one electrolyte disorder, hyponatremia and hypernatremia being the most common disorders. Similar to our study, they found that DM was associated with hyponatremia and hypomagnesemia, while HT was an independent risk factor for hypokalemia. Authors stated that hyponatremia and hypomagnesemia were independently associated with an increased risk of death. Unlike our results, they observed significant associations between use of diuretics, and benzodiazepines with particular electrolyte abnormalities. High prevalence of electrolyte abnormalities was also shown by Woyesa et al. (15). Forty-two percent of their patients with DM had at least one electrolyte abnormality. Some of the associations between comorbidities and electrolyte disorders may be bi-directional. For instance, patients with DM usually have a lower serum magnesium level, while hypomagnesemia itself is associated with a higher risk of DM (16).

Homeostasis of all electrolytes depends on the balance between gastrointestinal absorption and kidney excretion (17). Kidney functions appear to be the most prevailing factor to increase the frequencies of several electrolyte abnormalities in our study, including hyperkalemia, hypermagnesemia, hyperphosphatemia, and hypocalcemia. All of electrolyte abnormalities were mild in our study. However, sample sizes in each group were low, which questioned the representativeness of the sample hindering concrete conclusions. Malnutrition and drug exposures may be other crucial factors that may lead to several electrolyte imbalances. Deficiency of the majority of the ions, particularly hypophosphatemia and hypomagnesemia may in part occur secondary to poor oral intake. Yet, we could not demonstrate a significant association between malnutrition and various electrolyte disorders. Similarly, we expected to observe several associations between particular drug therapies and electrolyte disorders. Although some disorders were common in the case of usage several drugs, none of these associations reached a statistical significance. This might be explained by the multiple

coexistent factors for each electrolyte disorder. For instance, patients with CKD are more likely to have hyperkalemia. On the other hand, these subjects are more likely to receive loop diuretics which commonly cause hypokalemia. If the cause of CKD is DM, than the risk of hyperkalemia is increased due to hyporeninemic hypoaldosteronism. This is the likely explanation for the lack of observation of a significant association between hyperkalemia and drug exposures in subjects who have received renin-angiotensin-aldosterone system inhibitors, or hypokalemia with thiazides and loop diuretics. It is worth to note that considerable interrelationships may also exist across different electrolyte disorders.

### Study Limitations

Our study had several limitations. Given the retrospective design, a cause and effect relationship could not be established. Only single serum measurements was available. Some groups included quite low sample sizes questioning the representativeness of the study findings. There are many confounding factors that may cause electrolyte imbalance, and have different impact on functional dependence. Importantly, some of the electrolytes (potassium, magnesium, and phosphorus) are primarily involved in the intracellular compartment, which makes it hard to reach a solid conclusion. On the other hand, we used the same measurement methods which were routinely used in clinical practice while assessing such disorders. However, our study was the first to evaluate prevalence of various electrolyte abnormalities in the same elderly outpatient population, which was the main aim of this paper. This study had a small sample size for assessing frequency of electrolyte abnormalities, so our results should be confirmed by studies with larger sample sizes.

### Conclusion

Electrolyte abnormalities are common in outpatient elderly settings and are associated with dependency. Although hyponatremia is the most frequent electrolyte disorder, in total, magnesium abnormalities comprise the largest part and may require special attention.

### Ethics

**Ethics Committee Approval:** Bezmalem University Non-Interventional Research Ethics Committee (01.09.2020).

**Peer-review:** Externally peer reviewed.

### Authorship Contributions

Concept: C.H., R.K., Design: C.H., R.K., L.S., P.S., Data Collection or Processing: S.G.T., P.S., Analysis or Interpretation: C.H., S.G.T., R.K., L.S., P.S., Literature Search: C.H., S.G.T., Writing: C.H., L.S., P.S.

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