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Geriatric patients with acute kidney injury in the intensive care unit: the effect of vitamin B12 and albumin levels on survival

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ABSTRACT

Objectives: Acute kidney injury (AKI) is a common and critically important clinical entity in geriatric age group. In addition, higher mortality rates are seen in cases requiring intensive care treatment. We have aimed to investigate the effect of vitamin B12 and albumin levels on mortality in critically ill geriatric patients with AKI.

Methods: Geriatric patients hospitalised in the Intensive Care Unit with a diagnosis of AKI between 07.01.2014-07.01.2015 were retrospectively screened and included in the study. Two groups were formed from discharged and exited patients. General characteristics and laboratory values of the patients were scanned from the hospital archives and recorded. Statistically significant intergroup differences in terms of demographic characteristics, and biochemical values were determined by statistical analysis.

Results: A total of 103 patients, including 53 females were enrolled in the study, while 72.2% of the patients had prerenal AKI. The mortality rate was 47.57% in all patients. There was no difference between groups in terms of mortality rates, etiologic factors and KDIGO staging. Vitamin B12 was high and albümin was low the group who succumbed to death. In addition, mortality rates increased by 10% for every 100 units increase in vitamin B12 value and decreased by 22% for every 10 units increase in albumin value.

Conclusions: We have determined that an increase in albumin levels during clinical follow-up decreased mortality rates and an increase in vitamin B12 levels directly increased mortality rates. Hypoalbuminemia and high vitamin B12 levels were found to be independent predictive factors for mortality in AKI.

Keywords: Vitamin B12, albumin, acute kidney injury, geriatrics

The geriatric population is defined as the population of people aged 65 years and older [1]. With aging, morphological changes occur in the kidneys such as anatomical reduction in renal size and decrease in parenchymal volume, and functional changes such as decrease in renal blood flow and glomerular filtration rate (GFR). In addition, chronic diseases such as hypertension (HT), diabetes mellitus (DM), heart failure (HF) etc., which have a high prevalence in the elderly population, increase the risk of adverse structural and functional changes in the kidneys with aging [2]. As is known the incidence of acute kidney injury (AKI) increases in the elderly population compared to younger individuals [3]. AKI is defined as the development of functional abnormality in the kidneys within hours or days [4]. Functional ab-

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normality parameters include the rate and relative ratio of increase in serum creatinine levels and the amount of urine formed in a certain period of time. Three stages have been defined according to these parameters in the classification of KDIGO [5]. Renal dysfunction frequently improves in AKI and the prognosis is good. The geriatric population and the patients who need intensive care have higher mortality rates, need renal replacement therapy (RRT) more often and permanent loss of renal function is observed more frequently [6].

Albumin is a natural protein produced in the liver. Its half-life is 18 days and it has different physiologic effects and functions. The most important of these are maintenance of plasma oncotic pressure, and acid-base balance, hormone and drug transport, and regulation of the immune system.7 Albumin is also a negative acute phase reactant. A decrease in albumin levels below 30 g/L is defined as hypoalbuminemia and is frequently detected in critically ill patients [8].

Vitamin B12 is not produced in the body and must be taken from outside and its deficiency is associated with anemia and neuropsychiatric disorders [9]. Deficiency may be observed in nutritional disorders and gastrointestinal system diseases that cause malabsorption [10]. High vitamin B12 levels may be related to iatrogenic causes or may be observed in diseases including liver disease, polycythemia vera, leukemia and chronic kidney disease (CKD) [11]. In addition, a relationship between high vitamin B12 levels and inflammatory parameters has been shown [12].

In our study, we have aimed to investigate the effect of vitamin B12 and albumin levels on survival in geriatric patients with AKI who were hospitalised in the internal medicine intensive care unit.

METHODS

This study was planned as a retrospective screening study of geriatric patients with AKI hospitalized in the Internal Medicine Intensive Care Unit of Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital between 07.01.2014 and 07.01.2015.

Inclusion Criteria

Patients aged 65 years and older who were hospitalized in the internal medicine intensive care unit with a diagnosis of acute kidney injury were included in the study. The KDİGO (Kidney Disease: Improving Global Outcomes) guidelines were used for the diagnosis and staging of AKI [5].

Exclusion Criteria

Patients under 65 years of age, those who were discharged within the first 48 hours of their admission to ICU, and cases with a diagnosis of chronic renal failure who were on renal replacement therapy program were not included in the study.

Data Collection

Patients who were discharged from the intensive care unit (Group 1) and patients who did not survive (Group 2) were allocated into two separate groups. Besides, patients were also assessed in categories of prerenal, renal, and postrenal AKI according to the etiology of AKI.

Archival information was gathered concerning age, gender, comorbidities, diagnosis at intensive care unit admission, length of ICU stay, need for hemodialysis, and clinical outcomes of the patients. Relevant laboratory parameters [BUN, creatinine, uric acid, albumin, globulin, CRP, ferritin, B12, TSH, WBC, neutrophil, lymphocyte, Hgb, MCV, RDW, Plt, MPV] were recorded from the hospital information system. In addition, the albumin/globulin ratio and neutrophil/lymphocyte ratio (NLR) were calculated and recorded.

Ethical Statement

Ethical approval was received from the ethics committee of Kütahya Health Sciences University Faculty of Medicine with the decision dated 24.02.2021 and numbered 2021/03-15. The study was conducted by the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed with the help of SPSS version 17.0 program. The conformity of the variables to normal distribution was examined by histogram plots and Kolmogorov-Smirnov test. Mean, standard deviation, median, minimum, and maximum values were used in descriptive analyses. Categorical variables were compared with Pearson chi-square test. Mann-Whitney U test was used for non-normally dis-

tributed (nonparametric) variables between two groups. Kaplan-Meier analysis was used for univariate and Cox regression analysis for multivariate analysis. P-values below 0.05 were considered statistically significant.

RESULTS

A total of 103 patients, including 50 males and 53 females, were enrolled in the study. The mortality rate was 47.57% (n:49). The most common indications for admission were prerenal (72.2%), renal (22.33%) and postrenal (4.85%) AKI in respective percentages of patients. Etiologic factors for prerenal (infection: 65.33%, and dehydration: 20%), renal (infection: 72.73%, and toxic nephropathy 27.27%), postrenal AKI (% prostatic hyperplasia: 60%, and various malignancies: 40%) were identified in different proportions of patients as indicated.

According to KDIGO staging; patients had stage 1 (33.98%), stage 2 (36.89%), and stage 3 (29.13%) AKI. A total of 34 patients (33.01%) received renal replacement therapy (RRT) (Table 1).

General and etiologic factors were compared between the groups (Table 2). Any significant difference could not be found between groups in terms of gender, etiology, KDIGO staging and need for RRT when evaluated using the chi-square test.

Differences between the groups in terms of age, duration of hospitalization in days, and laboratory parameters were analyzed using the Mann-Whitney U test (Table 3). WBC, Neutrophil, NLR, RDW, MPV, B12, and CRP levels were statistically significantly higher in the non-surviving group. In addition, albumin, A/G ratio and creatinine levels were lower in this group.

Table 1. General characteristics and etiologies of AKI in all patients

		n	%
Sex	Male	50	48.54
	Female	53	51.46
Patient outcomes	Discharged	54	52.43
	Exitus	49	47.57
Types of AKI	Prerenal	75	2.82
	Renal	23	2.33
	Postrenal	5	4.85
Causes of prerenal AKI	Sepsis	49	65.33
	Dehydration	15	20.00
	Cardiovascular disease	7	9.33
	Chronic liver disease	4	5.33
Causes of renal AKI	Infection	16	72.73
	Toxic nephropathy	6	27.27
Causes of postrenal AKI	Prostatic hyperplasia	3	60.00
	Malignancy	2	40.00
KDIGO stages of AKI	Stage 1	35	33.98
	Stage 2	38	36.89
	Stage 3	30	29.13
Renal replacement therapy	Yes	34	33.01
	No	69	66.99

AKI=Acute Kidney Injury, KDIGO=Kidney Disease: Improving Global Outcomes Clinical Practice Guideline for Acute Kidney Injury

Table 2. Demographic characteristics and etiologic factors of AKI in both groups

		Group 1		Group 2		P value*
		n	%	n	%	
Sex	Male	27	54.00	23	46.00	0.756
	Female	27	50.94	26	49.06	
Types of AKI	Pre-renal	38	50.67	37	49,33	0.445
	Renal	12	52.17	11	7.83	
	Pos-trenal	4	80.00	1	20.00	
Causes of prerenal AKI	Sepsis	28	57.14	21	42,86	0.096
	Dehydration	8	53.33	7	46,67	
	Cardiovascular disease	2	28.57	5	71.43	
	Chronic liver disease	0	0.00)	4	100.00	
Causes of renal AKI	Infection	9	56.25	7	43.75	0.793
	Toxic nephropathy	3	50.00	3	50,00	
Causes of postrenal AKI	Prostatic hyperplasia	3	100.00	0	0.00	0.171
	Malignancy	1	50.00	1	50.00	
KDIGO stages of AKI	Stage 1	14	40.00)	21	60.00	0.40
	Stage 2	24	63.16	14	36.84	
	Stage 3	16	53.33	14	6.67	
Renal replacement therapy	No	37	53.62	32	46.38	0.729
	Yes	17	50.00)	17	50.00	

AKI=Acute Kidney Injury, KDIGO=Kidney Disease: Improving Global Outcomes Clinical Practice Guideline for Acute Kidney Injury

*Chi-Square Test

Cox regression analysis was performed with the values that were significantly correlated with mortality (Table 4). Accordingly, one unit increase in albumin value decreased the mortality risk by 0.221 times (95% CI: 0.062-0.789), and one unit increase in B12 value increased the mortality risk by 1.001 times (95% CI: 1.000-1.002).

DISCUSSION

In our study, we found that prerenal causes were more frequent in geriatric patients hospitalised in intensive care unit with the diagnosis of AKI, and high vitamin B12 and low albumin levels were directly associated with increased mortality risk. In addition, RDW, MPV and CRP levels were higher in the nonsurvived group.

With aging, structural and functional changes occur in the kidneys such as decreased parenchymal tissue, glomerulosclerosis, thickening of the glomerular basement membrane, decreased renal blood flow, and glomerular filtration rate [13, 14]. Because of these changes, the incidence of AKI is higher in the elderly population. In individuals over 70 years of age, AKI is detected 3.5 times more frequently than in younger individuals [5]. The mean age of the patients included in our study was 77.31±7.77 years. Development of AKI in elderly individuals is frequently due to iatrogenic and multifactorial causes. The most common causes are the use of nephrotoxic drugs or agents such as NSAIDs, diuretics, and radiocontrast agents [15]. In a multicenter study, the rate of development of AKI during hospitalization was found to be 48% in patients over 80 years of age with normal renal function tests at the time of hospitalization [16]. Prerenal azotemia is the second most common cause of AKI

Table 3. Comparison of laboratory parameters and demographic factors between groups

	Group 1		Group 2		P value*
	Mean±SD	Median	Mean±SD	Median	
Age (years)	76.98±7.12	78.00	77.67±8.49	79.00	0.624
Hospitalization (days)	10.74±8.72	8.00	15.88±19.15	9.00	0.352
WBC (10^3/µL)	12.80±5.98	11.30	15.36±7.15	14.70	**0.037**
Neutrophil (10^3/µL)	11.04±5.63	9.55	13.52 (6.86)	12.50	**0.032**
Lymphocyte (10^3/µL)	0.98±0.60	0.80	0.98±0.70	.60	0.501
NLR	14.88±10.00	12.42	20.04±14.48	16.08	**0.090**
Hemoglobin (g/dL)	11.46±2.19	11.20	11.42±1.90	11.60	0.840
RDW (%)	16.08±2.51	15.30	17.57±2.93	16.60	**0.001**
Platelets (10^3/µL)	238.63±111.94	234.00	227.76±165.24	203.00	0.170
MPV (fL)	8.55±1.41	8.20	9.21±1.26	9.30	**0.003**
MCV (fL)	87.30±5.62	87.40	88.04±7.55	86.80	0.820
Uric acid (µmol/L)	9.32±3.53	9.00	8.77±3.77	8.00	0.265
Albumin (g/dL)	31.2±4.4	31.0	27.4±5.9	27.0	**0.000**
A/G Ratio	1.08±0.22	1.06	0.97±0.31	0.96	**0.008**
Ferritin (µg/L)	323.26±321.31	263.50	544.09±511.80	270.00	0.071
VitaminB12 (pg/mL)	614.62±491.82	446.50	863.67±533.41	853.00	**0.038**
TSH (mIU/L)	1.70±2.51	.79	1.90±3.15	1.08	0.522
CRP (mg/L)	102.00±88.22	79.90	132.86±85.47	124.30	**0.021**
HCO_3 (mmol/L)	19.46±6.15	19.15	18.17±6.73	18.70	0.333
Urea (mmol/L)	189.44±104.36	162.50	155.22±68.47	151.00	0.137
Creatinine (mmol/L)	4.57±3.72	3.32	3.00±2.12	2.50	**0.011**
BUN (mg/dL)	89.11±45.15	76.50	71.96±32.23	71.00	0.060
BUN/Crea Ratio (%)	24.55±11.12	23.95	29.02±12.72	26.66	0.090

WBC=White Blood Cell, NLR=Neutrophil-to-Leucocyte Ratio, RDW=Red Cell Distribution Width, MPV=Mean Platelet Volume, MCV=Mean Corpuscular Volume, A/C= Albumin/Globulin Ratio, TSH=Thyroid Stimulating Factor, CRP=C-reactive Protein, BUN=Blood Urea Nitrogen, SD=Standard Deviation

*Mann- Whitney U Test

[17]. Dehydration (fluid loss through gastrointestinal tract, diuretic use, and decreased fluid intake, etc.) and decreased effective plasma volume (sepsis, and heart failure, etc.) are the causes of prerenal azotemia. Some studies have shown that sepsis is the most common indication for hospitalisation of the patients with AKI in the intensive care unit [18, 19]. In our study, prerenal causes were found more frequently in accordance with the literature. Among prerenal causes, sepsis was the most frequently detected cause and no significant difference was found in mortality rates regarding different etiologic causes of AKI.

Albumin plays an essential role in the maintenance of serum oncotic pressure and also has regulatory functions on the immune system [7]. Serum albumin levels may decrease in severe inflammations, in cases where albumin synthesis decreases due to hepatocyte injury and in cases of increased albumin depletion through renal route [20]. Hypoalbuminemia is known to be associated with increased mortality and morbidity rates independent of the underlying disease [21]. A meta-analysis of 90 studies conducted in crit-

Table 4. Biochemical parameeters affecting mortality (Cox Regression analysis)

	B	SE	P value	Exp(B)	95,0% CI for Exp(B)	
					Lower	Upper
WBC	-0.403	0.215	0.061	0.668	0.439	1.018
Neutrophil	0.443	0.233	0.057	1.557	0.987	2.457
RDW	-0.004	0.082	0.958	0.996	0.848	1.169
MPV	0.017	0.171	0.921	1.017	0.728	1.422
Albumin	-1.512	0.651	**0.020**	0.221	0.062	0.789
A/G ratio	0.485	0.816	0.552	1.624	0.328	8.043
Vitamin B12	0.001	0.000	**0.043**	1.001	1.000	1.002
CRP	-0.002	0.003	0.347	0.998	0.992	1.003
Creatinine	-0.094	0.129	0.466	0.910	0.708	1.171

WBC=White Blood Cell, RDW=Red Cell Distribution Width, MPV=Mean Platelet Volume, MCV= Mean Corpuscular Volume, CRP=C-reactive Protein

ically ill patients hospitalised in intensive care units, has shown that a 10 g/L decrease in albumin level caused a 137% increase in mortality rates and a 71% increase in hospital stay [22]. In another study, it was shown that low serum albumin level was a significant independent factor predicting the development of AKI [23]. In our study, serum albumin levels were significantly lower in the nonsurvived group. In addition, mortality rates decreased by 22% for every 10 g/L increase in serum albumin levels. In parallel with other studies conducted in critically ill patients, serum albumin was found to be an independent factor predicting mortality in critically ill geriatric patients diagnosed with AKI.

Although many studies have been conducted on health problems that may develop due to vitamin B12 deficiency, limited information is available on health problems that may develop due to its excess. B12, a water-soluble vitamin, plays a critical role in maintaining cellular functions, erythrocyte formation and metabolism of homocysteine [10]. It is now known that increased serum vitamin B12 levels are associated with systemic inflammatory response syndrome (SIRS), and impaired liver and kidney functions [24]. However, the effect of increased serum vitamin B12 levels in the development of AKI is not known exactly. In various studies elevated vitamin B12 levels have been associated with severe degrees of inflammation. Corcoran *et al*. [25] showed that increased CRP levels were correlated with high vitamin B12 levels in intensive care unit patients.25 Similarly, it has been showed that high vitamin B12 levels were associated with increased CRP levels. These findings suggest that increased vitamin B12 levels with their toxic inflammatory effects may induce development of kidney damage. In a multicenter study by House *et al*. [26], a decrease in GFR was observed after administration of high-dose vitamin B complex (containing vitamin B12) to patients with diabetic nephropathy. It was shown that increased serum vitamin B12 levels elevate the risk of developing AKI in patients undergoing liver transplantation and vitamin B12 level was a predictive factor for the development of AKI [26]. Besides relatively higher vitamin B12 levels were associated with increased rates of hospital mortality in adult patients [27]. As a result of these studies, it is obvious that vitamin B12 elevation is not innocent and further studies are needed to reveal its adverse effects. In our study, significantly higher serum vitamin B12 levels were detected in the nonsurvived patient group. It was also shown that every 100 unit increase in serum vitamin B12 levels caused a 10% increase in mortality rates. According to these results, it can be said that vitamin B12 level is an independent predictive factor for mortality. It is possible that extremely high serum vitamin B12 levels may increase mortality rates by inducing the development and exacerbation of AKI and by contributing to the exacerbation of inflammation.

Limitations

Our study has some limitations. Retrospective design and small patient group can be listed. In addition, the fact that the effect of additional comorbid diseases could not be fully evaluated due to its retrospective design can be considered as a limitation. There is a need to support the findings with large patient groups and prospective studies.

CONCLUSION

It is known that AKI is a frequently detected clinical condition among inpatients, and morbidity and mortality rates are higher both among patients hospitalised in the intensive care unit and in the geriatric age group. In the geriatric age group, the presence of additional parameters that will help in the evaluation of treatment efficacy and disease severity and predict mortality is thought to aid clinicians in patient follow-up.

It should be known, and taken into consideration that high vitamin B12 levels may exert toxic effects in AKI and increase mortality rates in patients with AKI. It is necessary to be more careful about vitamin B12 replacement in the geriatric age group.

Serum albumin levels decrease in critically ill patients and the presence of infection. It should be known that a low albumin level will have a negative effect on the clinical status of patients with potential development of immune system defects, while an increase in serum albumin levels has a mortality-reducing effect. In geriatric patients hospitalised in the intensive care unit, applications to increase albumin levels should always be evaluated and albumin replacement should be considered frequently in case of need.

Authors' Contribution

Study Conception: SE, TPK; Study Design: SE, TPK; Supervision: SE, TPK; Funding: SE, TPK; Materials: SE, TPK; Data Collection and/or Processing: SE, TPK; Statistical Analysis and/or Data Interpretation: SE, TPK; Literature Review: SE, TPK; Manuscript Preparation: SE, TPK and Critical Review: SE, TPK.

Ethics Approval

Ethical approval was received from the ethics committee of Kütahya Health Sciences University Faculty of Medicine with the decision dated 24.02.2021 and numbered 2021/03-15.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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