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Some Renal Marker Levels in Geriatric Rats

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ABSTRACT The aim of this study was to determine Neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), cystatin C (Cyc-c), and interleukin-18 (IL-18) levels which are frequently used as kidney biomarkers in geriatric rats and to compare with those in young rats. For this purpose, 12 geriatric Wistar albino rats (30-36 months old) (six males and six females) and 12 (2-3 months old) (six males and six females) Wistar albino rats were used in this study. 24-hour urine samples of all groups were collected, and blood was collected for biochemical analysis under anesthesia. The mean body weight of the geriatric rats was statistically higher than the young rats ($p<0.001$). The 24-hour urine volume was also statistically higher in geriatric rats than in young ones ($p<0.01$). Serum Cyc-c ($p<0.05$), KIM-1 ($p<0.01$), glucose ($p<0.05$), total protein (TP) ($p<0.001$) and creatinine (Crea) levels in geriatric rats ($p<0.001$) were statistically higher than the young rats. However, there was no statistically significant difference in IL-18, NGAL, and urea (mg/dL) levels. In the 24-hour urine sample, although Cyc-c ($p<0.05$), Urea ($p<0.01$), Crea ($p<0.01$) and protein ($p<0.001$) levels in geriatric rats were statistically significant compared to young rats; there was no statistically significant difference in KIM-1, IL-18, and NGAL levels. As a result, in geriatric rats, the diagnosis, treatment, and prognosis must be evaluated by considering Crea, glucose, urea, TP levels, and KIM-1, Cyc-C changes. It was concluded that blood Crea, glucose, urea, TP levels as well as KIM-1, Cyc-C levels, and urinary Cyc-C levels should also be considered in future studies.

Keywords: *Biomarkers, Kidney, Rats.*

ÖZ

Geriatrik Ratlarda Bazı Böbrek Biyobelirteç Düzeyleri

Bu çalışmada ileri yaşlı ratlarda, son yıllarda böbrek belirteci olarak sıkça kullanılan neutrophil gelatinase-associated lipocalin (NGAL), kidney ınjury molecule-1(KIM-1), sistatin C (Cyc-c) ve interleukin-18 (IL-18) düzeylerinin belirlenmesi ve bu düzeylerin genç ratlardakilerle kıyaslanması hedeflenmiştir. Bu amaçla çalışmamızda 12 Adet geriatrik Wistar albino rat (30-36 aylık) (6 erkek ve 6 dişi) ile 12 adet (2-3 aylık) (6 adet erkek ve 6 adet dişi) Wistar albino rat kullanıldı. Yaşlı ratların ortalama canlı ağırlıkları genç ratlara göre istatistiksel olarak önemli derecede yüksekti ($p<0.001$). Çıkartılan 24 saatlik idrar miktarı yaşlı ratlarda gençlere göre istatistiksel olarak yüksekti ($p<0.01$). Geriatrik ratlarda Serum Cyc-c ($p<0.05$), KIM-1 ($p<0.01$), glikoz ($p<0.05$), total protein (TP) ($p<0.001$) ve kreatinin (Crea) düzeyleri ($p<0.001$) istatistiksel olarak genç ratlarınkine göre daha yüksekti. Ancak IL-18, NGAL ve Üre (mg/dL) düzeylerinde istatistiksel olarak anlamlı bir fark bulunamadı. Geriatrik ratlarda, 24 saatlik idrar örneğinde Cyc-c ($p<0.05$), üre ($p<0.01$), Crea ($p<0.01$) ve Protein ($p<0.001$) düzeyleri genç ratlara göre istatistiksel olarak anlamlı olmakla birlikte; KIM-1, IL-18 ve NGAL düzeylerinde istatistiksel olarak anlamlı fark yoktu. Sonuç olarak geriatrik ratlarda KIM-1, Cyc-C değişikliklerinin yanı sıra Crea, glucose, urea, TP düzeyleri dikkate alınarak tanı, tedavi ve prognoz değerlendirilmelidir. Ayrıca kan Crea, glukoz, üre, TP düzeylerinin yanı sıra KIM-1, Cyc-C düzeyleri ve idrar Cyc-C düzeylerinin de ileriki çalışmalarda dikkate alınması gerektiği düşünülmektedir.

Anahtar Kelimeler: *Biyobelirteçler, Böbrek, Ratlar.*

INTRODUCTION

The probability of reaching advanced age in animals also increases due to the developing technology and treatment applications. Gerontology aims to struggle with diseases that may occur with advancing age.

In humans, geriatric rat is defined at the age of 65 and above (Rosenthal and Kavic 2004; Özbek et al. 2008; Kumsar and Yılmaz 2014; Aydemir and Çetin 2019), whereas in laboratory rats, the age of 2 years and above is defined as geriatrics (Quinn 2005; Sengupta 2011; Andreollo et al. 2012). There are changes in physiological

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and biochemical values in humans compared to healthy young people in the advanced age period. With aging, organ functions decrease partially; however, it is stated that this rate of decrease differs according to both the individual and the systems (Ashworth et al. 1960; Döventaş and Döventaş 2012). Rats are significant models for humans in geriatric studies. It is reported as 16.4 rat days are equal to 1 human year between human and rat age by taking the average human lifespan of 80 years and the average laboratory rat lifespan of 3 years (Quinn 2005; Sengupta 2011; Andreollo et al. 2012).

Although the risk of disease and disability increases markedly with advancing age, early diagnosis of disability and death due to many chronic disorders helps take preventive measures (Rosenthal and Kavic 2004; Holly 2009; Kumsar and Yılmaz 2014; Aydemir and Çetin 2019).

Many organs and systems are affected by advancing age. One of them is the kidneys (Çapar and Çapar 2018). Changes in physiological and biochemical parameters are observed depending on the diseases that develop with advancing age (Gereklioğlu et al. 2007; Özbek et al. 2008; Özcan and Kapucu 2014).

Some biochemical parameters such as glomerular filtration rate (GFR) and albumin, creatinine, and urea rates are routinely evaluated in renal involvement (Başbuğan and Ağaoğlu 2018). In geriatric rats; renal 1-α hydroxylase, 1,25-(OH)2D levels, RAS – (Renin-angiotensin system); ET – (endothelin); PAF – (platelet-activating factor) – ROS (reactive oxygen species). Advanced glycation end products (AGE) (Bendayan 1998; Jerkić et al. 2001; Huang, et al. 2009). However, it has been notified that NGAL, KIM-1, Cyc-c, and IL-18 levels, which are more specific than these parameters and have been used recently, reveal renal damage early (Ichimura et al. 1998; Mori et al. 2005; Vaidya and Bonventre 2006; Faubel et al. 2007; Niemann et al. 2009; Duymaz et al. 2017; Alwan and Al-Saeed 2023; Hagiwara et al. 2023; Huang et al. 2023; Paul et al. 2023; Xing et al. 2023).

NGAL is a 25 kDa molecular weight member of the lipocalin family and is produced by inflammatory cells, adipose tissue, liver, colon, lung, and renal epithelium. The most well-known functions of NGAL are iron transport, regulation of apoptosis, infection control, structural development, and renal recovery. NGAL is a new biomarker for diagnosing very early stages of acute kidney injury (Kjeldsen et al. 1993; Yang et al. 2003; Devireddy et al. 2005, Gwira et al. 2005; Mori et al. 2005).

KIM-1 gene and protein expression, which is a type 1 cell membrane the glycoprotein cannot be detected in healthy kidneys and urine, and thus, KIM-1 mRNA is rapidly synthesized following damage. The KIM-1 protein is highly localized and produced in the apical membranes of differentiated proximal tubule cells of human and rodent kidneys after ischemia and toxic injury (Ichimura et al. 1998; Huang et al. 2023; Xing et al. 2023). High urinary KIM-1 expression has been associated with adverse clinical outcomes in patients with acute kidney injury (Liangos et al. 2007).

Interleukin-18 has been defined as a proinflammatory factor induced by interferon γ (Faubel et al. 2007). IL-18 is associated with many renal diseases (Melnikov et al. 2001; Alwan and Al-Saeed 2023). In humans, IL-18 is one of the early markers of renal tubular diseases. (Parikh et al. 2005) It has been reported that the IL-18 level is 90% specific and sensitive for diagnosing acute renal failure in humans (Melnikov et al. 2001; Faubel et al. 2007).

Another renal marker, Cyc-c, is a protease inhibitor synthesized and released from all nuclear cells (Han et al. 2002). Moreover, it is aimed to compare the change according to gender and age. Although studies related to aging in humans were found in the literature review, no similar study was found on rats.

MATERIAL AND METHODS

This study was approved by the Yuzuncu Yil University Animal Experiments Local Ethics Committee (Date: 28/01/2021; Decision number: 2021/05-17). The study was carried out at Yuzuncu Yil University Experimental Medicine Application and Research Center. In this study, 12 geriatric rats (average age of 30-36 months; 32.33 months) (6 males and six females) fed ad libitum with standard rat pellet food and ordinary tap water were used in an environment of 22-24 °C average temperature, 40-60 humidity, and reverse lighting, which was not included in any experimental study before and again, 12 Wistar albino rats (2-3 months average, 2.58 years old) (6 males and six females) fed with standard rat pellet feed and ordinary tap water ad libitum at 22-24 °C average temperature and 40-60 humidity environment, which were not included in any experimental study before, were used. Groups were formed from animals that did not show any clinical signs of disease in the animals included in the study. Feed and water consumption of the last five days and urine and stool samples of the previous 24 hours were evaluated to create a sample.

After collecting urine with a metabolic cage (Tecniplast2®), 24-hour urine samples from the animals included in the study were sacrificed with xylazine 10 mg/kg IP (2% Rompun® Bayer) and Ketamine (HCl) (10% Alfamine® Atafen) 75 mg/kg IP injectable anesthetics while the rats were under anesthesia by the high blood collection method. Serum was obtained from the obtained blood and renal damage markers NGAL (Catalog No: SG-20801, SinoGenClon Biotech), KIM-1 (Catalog No: SG-20751, SinoGenClon Biotech), Cyc-c (Catalog No: SG-720197, SinoGenClon Biotech) and IL-18 (Catalog No. SG-20281, SinoGenClon Biotech) levels were determined with species-specific ELISA kits. Furthermore, urea, creatinine, albumin (Alb), and total protein (TP) levels, which are among the routine parameters of the renal and blood glucose levels, were measured with Abbott, Architect ci16200.

Statistical Analysis

Statistical interpretation of the findings was made with the SPSS 21.0 computer package program, and the arithmetic means and standard deviations of all parameters were calculated. Kolmogorov-Smirnov normality test was performed. "One-way analysis of variance (ANOVA)" test to determine the difference between the groups, and to determine from which group the differences originate; "Duncan" test, one of the multiple comparison tests, was used. Differences at the $p<0.05$ level were considered significant.

RESULTS

The physiological activities of the young rats were normal, and their fur was shiny. Their feed and water consumption were normal, and their movements were swift and agile. While hair loss was observed in elderly rats in the geriatric category, their physiological activities were relatively slow compared to young ones.

Table 1: Live weight of rats, feed and water consumption, urine and stool amounts.

Parameters	Elderly (n:12)	Young (n:12)	p value
Live Weight (gr)	279.50±9,22	173.58±14,60	**0.001**
Water Consumption (ml/24 hours)	32.33±1.85	32.66±1,22	0.882
Feed Consumption (gr/24 hours)	15.72±1.80	17.27±0,90	0.453
Urine amount (ml/24 hours)	15.66±1.66	9.33±0,80	**0.002**
Fecal amount (gr/24 hours)	8.61±1.35	7.11±0,59	0.318

The difference between the values on the same line is statistically significant (*; p<0.05) (**; p<0.01), (***; p<0.001).

Table 2: Live weight, feed and water consumption, urine and stool amounts of rats by gender.

Parameters	Elderly Male (n:6)	Elderly Female (n:6)	Young Male (n:6)	Young Female (n:6)
Live Weight (gr)	300.67±21.19[a]	258.33±26.84[b]	179.50±13.59[c]	167.67±14.16[c]
Water Consumption (ml/24hours)	18.50±8.37 [a]	12.67±5.09 [a]	18.78±2.43 [a]	15.75±5.28 [a]
Feed Consumption (gr/24hours)	30.00±7.88 [a]	35.78±7.03 [a]	33.33±5.00 [a]	31.00±5.01 [a]
Urine amount (ml/24 hours)	13.78±2.06[a]	17.56±1.61[a]	7.11±0.48[c]	11.00±0.52[b]
Fecal amount (gr/24 hours)	11.40±5.97 [a]	5.67±3.31 [a]	8.11±2.14 [a]	5.63±2.26 [a]

Different letters on the same line are statistically significant (p<0.05).

Table 3: Serum Cyc-c, KIM-1, NGAL, IL-18, urea, creatinine (Crea), TP, Alb, and glucose levels in rats.

Parameters	Elderly (n:12)	Young (n:12)
Cyc-c (ng/mL)	41.85±4.87	35.79±7.60*
KIM-1 (pg/mL)	86.87±5.97	74.48±9.11**
NGAL (ng/mL)	0.66±0.08	0.66±0.08
IL-18 (pg/mL)	91.45±11.33	88.17±8.52
Urea (mg/dL)	46.40±8.82	45.08±3.57
Crea (mg/dL)	0.61±0.06	0.49±0.02***
TP (g/L)	67.36±4.45	58.60±1.89***
Alb (g/L)	28.27±3.13	30.30±1.05
Glucose(mg/dL)	113.38±5.73	97.50±2.52*

The difference between the values on the same line is statistically significant (*; p<0.05) (**; p<0.01), (***; p<0.001).

Table 4: Cyc-c, KIM-1, NGAL, IL-18, urea, Crea, and protein levels in urine samples of rats.

Parameters	Elderly (n:12)	Young (n:12)
Cyc-c (ng/mL)	47.02±5.68	42.49±4.11*
KIM-1(pg/mL)	83.62±7.88	85.18±8.07
NGAL (ng/mL)	0.79±0.11	0.86±0.15
IL-18 (pg/mL)	5.78±1.97	4.51±1.47
Urea (mg/dL)	3145.00±493.14	1998.10±706.99**
Crea (mg/dL)	65.82±20.41	30.05±17.00***
Protein (g/L)	50.33±15.39	27.60±10.38**

The difference between the values on the same line is statistically significant (*; p<0.05) (**; p<0.01), (***; p<0.001).

According to the results, while there was no statistical difference between the old and young rats in the consumption of Water and Feed and the amount of stool removed, statistically significant differences were found between body weight and urine volume (p<0.001 and p<0.01).

A statistically significant difference (p<0.05) was found between the mean body weights of the old and young rats according to their genders. In the comparison between 24-hour feed and water consumption, urine and stool amounts, on the other hand, there was a significant difference solely in the volume of urine.

A statistically significant difference was detected in serum Crea (p<0.001), TP (p<0.001), Cyc-c (p<0.05), KIM-1 (p<0.01), and Glucose (p<0.05) levels of old and young rats. These values were higher in the elderly than in the young.

A statistically significant difference was found between the serum Crea (p<0.001) protein (p<0.01) and Cyc-c (p<0.05) levels in the urine samples of old and young rats. These values were higher in the elderly than in the young.

DISCUSSION AND CONCLUSION

The age of 2 years and above is defined as geriatrics in laboratory rats (Quinn 2005; Sengupta 2011; Andreollo et al. 2012). There are changes in physiological and biochemical values in humans compared to healthy young people in the advanced age period. With aging, organ functions decrease partially; however, it is stated that this rate of decrease differs according to both the individual and the systems (Ashworth et al. 1960; Döventaş and Döventaş 2012).

Rats consume an average of 15-25 g (5-6 g for 100 g CA) feed and 30-45 ml (10-12 ml for 100 g CA) water per day (İde 2003). The average water and feed consumption of the rats included in this study was similar to the

researcher's statement (İde 2003) (Table 1). Basbugan and Ağaoğlu (2018) stated that male rats consume more feed and water than females in their study. However, there was a decrease in water and feed consumption compared to live weight in the older group, expressed as geriatric. It is considered that this may be due to the metabolism rate, which is affected by aging, as stated by researchers (Döventaş and Döventaş 2012).

The decrease in physiological activity that comes with aging affects feed and water consumption and the volume of urine and stool excreted. As seen in this study, the live weights of the old rats were statistically significantly higher than the young rats. This is proof that young rats are still in the developmental stage. In the comparison made according to feed and water consumption rates based on the CA determined for rats by IDE 2003, it was determined that older rats consumed less feed and water. Although there is no statistical significance between water consumption, metabolism slows down in the elderly due to aging. Nevertheless, when the urine volume excreted was examined, it was identified that the older rats produced a statistically significant volume of urine compared to the young rats (Table 2). As researchers (Döventaş and Döventaş 2012) stated, we think that this situation may develop due to the decrease in tubular uptake of water with aging.

Table 5: Serum Cyc-c, KIM-1, NGAL, IL-18, urea, Crea, TP, Alb and glucose levels in all group rats.

Parameters	Elderly Male (n:6)	Elderly Female (n:6)	Young Male (n:6)	Young Female (n:6)
Cyc-c (ng/mL)	43.28±3.20 [a]	40.65±5.69 [a]	41.70±5.71[a]	31.89±6.17 [b]
KIM-1 (pg/mL)	86.94±7.33 [a]	86.81±5.65 [a]	73.89±7.53 [b]	74.87±10.71 [b]
NGAL (ng/mL)	0.63±0.07 [a]	0.70±0.10 [a]	0.67±0.09 [a]	0.64±0.08 [a]
IL-18 (pg/mL)	95.49±13.3 [a]	88.09±9.16 [a]	90.62±11.18 [a]	86.14±5.85 [a]
Urea (mg/dL)	39.75±2.21 [a]	50.83±8.84 [b]	46.00±4.63 [a,b]	43.93±1.47 [a,b]
Crea (mg/dL)	0.64±0.06 [a]	0.58±0.54 [a]	0.47±0.16 [b]	0.51±0.02 [b]
TP (g/L)	6.46±0.43 [a]	6.96±0.32 [a]	5.90±0.24 [b]	5.82±0.13 [b]
Alb (g/L)	2.64±0.24 [a]	2.98±0.29 [b]	3.06±0.11 [b]	3.00±0.10 [b]
Glucose(mg/dL)	114.83±24.10 [a]	112.14±19.15 [a]	92.33±1.21 [b]	102.67±10.13 [a]

The difference between different letters on the same line is statistically significant ($p<0.05$).

Table 6: Cyc-c, KIM-1, NGAL, IL-18, urea, Crea, protein levels in all group rat urines.

Parameters	Elderly Male (n:6)	Elderly Female (n:6)	Young Male (n:6)	Young Female (n:6)
Cyc-c (ng/mL)	49.76±4.20 [a]	44.29±5.92 [a,b]	43.84±4.27 [a,b]	41.13±3.80 [b]
KIM-1 (pg/mL)	85.88±8.29 [a]	81.36±7.46 [a]	83.42±6.20 [a]	86.94±9.86 [a]
NGAL (ng/mL)	0.76±0.14 [a]	0.82±0.06 [a]	0.92±0.19 [a]	0.78±0.03 [a]
IL-18 (pg/mL)	6.23±2.48 [a]	5.33±1.54 [a]	5.41±1.04 [a]	3.60±1.37 [a]
Urea (mg/dL)	2899.75±435.56 [a, b]	3472.00±405.34[a]	2132.60±342.36 [b, c]	1863.60±980.9[c]
Crea (mg/dL)	55.72±18.87 [a, b]	72.56±20.00 [a]	28.32±7.64 [c]	31.48±22.93 [b, c]
Protein (g/L)	47.26±14.62 [a]	54.17±17.63 [a]	28.20±9.11 [b]	26.90±12.83 [b]

The difference between different letters on the same line is statistically significant ($p<0.05$).

Routine biochemical parameters are also affected by aging (Sorva 1992; Ham 2007). Sorva (1992) indicates that hypoalbuminemia may develop with aging. In the comparison made between serum urea, Crea, TP, Alb, and glucose levels between old rats and young rats, the amount of TP was statistically significantly higher in the elderly than in the young in this study. (Table 3). As this situation can lead to dehydration, which is one of the biggest problems of old age, as a result of the decrease in the water holding capacity and water consumption from the kidneys due to aging, it is thought that an increase in TP level in the elderly may be relative. As can be seen from the urine analysis, the urine protein ratio is statistically significantly higher in the elderly than in the young (Table 4). This result is in line with the data of Döventaş and Döventaş (2012) that there may be a decrease in TP and Alb levels and a slight increase in globulin levels due to aging. It also supports the fact that the urea, Crea, and protein ratios in the urine analysis of the elderly are statistically significantly higher than those of the youngs. The most significant factor of this determination, as stated by researchers (Ashworth et al. 1960; Döventaş and Döventaş 2012), is thought that the kidney's water-holding capacity decreases due to aging, resulting in increased urine and increased creatine level with urine, rapid urination of urea from the circulation and protein leakage of the kidney as a result of advanced aging.

Among the parameters such as Cyc-c, KIM-1, NGAL, IL-18, which have been used as kidney damage markers in recent years, KIM-1, NGAL, IL-18 are evaluated as indicators of acute inflammation. (Ichimura et al. 1998; Parikh et al. 2005; Liangos et al. 2007; Kuwabara et al. 2009; Zhang et al. 2011; Duymaz et al. 2017; Dirik et al. 2021).

It has been reported that thickening of the glomerular and tubular basement membranes with advancing age will lead to the development of hypertension and a change in the amount or quality of the glomerular filtrate (Ashworth et al. 1960).

IL-18, which is associated with many renal diseases, is one of the early markers of renal tubular disorders. IL-18 level has been reported to be 90% specific and sensitive for the diagnosis of acute renal failure in humans

(Melnikov et al. 2001; Parikh et al. 2005; Faubel et al. 2007).

In this study, no statistically significant difference was found in IL-18 levels in both serum and urine analyses of old and young rats (Table 3, Table 4, Table 5, and Table 6). It is considered that the damage in the tubules due to aging is not in the acute phase but maybe in the chronic phase and depending on reaching this period; it regresses to the same level as the young rat values.

In this study, no statistically significant difference was found in the NGAL level, a biomarker in diagnosing very early stages of acute kidney injury, both serum, and urine analysis of old and young rats (Table 3, Table 4, Table 5 and Table 6). This suggests that the damage to the kidneys due to aging is not in the acute stage or is at a chronic level.

Cystatin C is a protease inhibitor synthesized and released from all nuclear cells (Han et al. 2002). Cyc-C is filtered by the glomerulus and catabolized by proximal tubular cells due to its low molecular weight (Westhuyzen 2006; Ledoux et al. 2007). Cystatin C is not affected by the body skeletal system. It has been reported that it does not differ depending on gender and age (Grubb et al. 1992; Laterza et al. 2002; Zhang et al. 2011). In this study, these levels were 41.85±4.87 ng/mL in old rats and 35.79±7.60 ng/mL in young rats. Urine Cyc-C level was 47.02±5.68 ng/mL in the elderly and 42.49±4.11 ng/mL in young rats (Table 3, Table 4). In the light of these data, the Cyc-C level was statistically significant in both serum and urine levels ($p<0.05$) (Table 3). This situation may be an indication of changes in renal functions due to aging in rats. When evaluated in terms of gender, the level detected in young females was statistically lower than the levels of old females, old males, and young males ($p<0.05$) (Table 5 and Table 6). Although this situation does not coincide with the researchers' statement (Grubb et al. 1992; Laterza et al. 2002; Zhang et al. 2011) that Cyc-C is not affected by age and gender, the fact that there is no statistical difference between the levels of young males and older males and females supports this statement of the researchers (Grubb et al. 1992; Laterza et al. 2002; Zhang et al. 2011). We think that the reason for this difference in females may be due to individual data.

KIM-1 is a type 1 cell membrane glycoprotein. Following damage to the KIM-1 gene and protein expression, KIM-1 mRNA is rapidly synthesized. The KIM-1 protein is highly localized and produced in the apical membranes of differentiated proximal tubule cells of human and rodent kidneys after ischemia and toxic injury (Ichimura et al. 1998). Vaidya et al. (2009) reported that the level of KIM-1 could not be detected before and 6 hours after surgery, peaked at the 24th hour after surgery (4800 pg/ml) and then decreased. In this study, serum KIM-1 level was statistically higher in old rats than in young rats ($p<0.01$). No difference was detected in urine levels. The difference between the sexes was also insignificant. This is an indication that renal functions are affected in the older ones. Although the serum level is high in the older rats in the evaluation of urine analysis, it is thought that KIM-1 does not pass into the urine at a significant level. The main reason for this is that it is highly localized in the apical membranes of proximal tubule cells, as stated by Ichimura et al. (1998).

A statistically significant difference was found in Cyc-c and KIM-1 compared the renal damage markers such as serum Cyc-c, KIM-1, NGAL, IL-18 in old and young rats (Table 3). This suggests that, as researchers Ashworth et al. 1960 stated, changing physiological and metabolic effects, which reflect aging, may trigger an increase in serum Cyc-c and KIM-1 activity with a negative impact on the glomeruli. Moreover, it is considered that there may be a disruption in the catabolism of Cyc-c due to the negative changes in the functions of the tubules due to aging. It is understood that the glomerulus is negatively affected by the urine level produced by the old rats and the protein content of the urine.

In conclusion, it was determined that there are adverse effects on physiological activity and kidneys in the geriatric period. As a result of these effects, serum KIM-1, Cyc-C, creatinine, glucose, and TP levels increase. However, there is no statistically significant change in NGAL and IL-18 levels. In terms of urine analysis, it was observed that there were increases in urine Cyc-C, Crea, Protein levels in old rats. Nevertheless, no statistically significant increases in KIM-1, NGAL, and IL-18 levels. In the light of these results, it is concluded that the diagnosis, treatment, and prognosis should be evaluated by considering the serum Crea, Glucose, Urea, TP levels, KIM-1, Cyc-C levels and the changes in the urine Cyc-C, Crea, Urea and Protein levels of the patients in the geriatric period.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

Idea / Concept: YB, AFK, ENO, UÖ
Supervision / Consultancy: NY, AFK, UÖ
Data Collection and / or Processing: YB, NY, AFK, ENO, UÖ
Analysis and / or Interpretation: YB, NY, AFK, ENO, UÖ
Writing the Article: YB, ENO
Critical Review: NY, AFK, UÖ

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