Serum chemerin level in chronic kidney disease

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Background
Chronic kidney disease (CKD) is a progressive loss in renal function over a period of months or years. In the metabolic association of an elevated circulating chemerin level in the context of uremia demonstrate that high chemerin levels predict a better survival in CKD patients. The aim of the study was to measure serum chemerin and to correlate it with other parameters in CKD patients.
Patients and methods
This study was conducted on 40 patients with CKD, including 20 patients with end-stage renal disease under regular hemodialysis and 20 patients with renal impairment on conservative therapy who have not started hemodialysis, and 22 apparently healthy participants serving as the control group. Human chemerin is determined by sandwich enzyme immunoassay.
Results
There is a highly statistically significant difference in mean serum chemerin and mean serum high-sensitivity C-reactive protein (hs-CRP) in the patient groups in comparison with the control group. In addition, there was a highly statistically significant difference between control group, under hemodialysis group, and renal impairment group as regards serum chemerin and serum hs-CRP. A positive correlation between serum chemerin and hs-CRP studied in the under hemodialysis group, renal impairment group, and in all patients' group.
Conclusion
A significantly higher chemerin level in patients with impaired kidney function compared with the normal control group, and a high increase in patients under hemodialysis compared with the other two groups.

Keywords:
chemerin, chronic kidney disease, high-sensitivity C-reactive protein, insulin

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Introduction

Chronic kidney disease (CKD), also known as chronic renal disease, is a progressive loss in renal function over a period of months or years [1]. CKD is defined as kidney damage or glomerular filtration rate (GFR) less than 60 ml/min/l.73 m^2 for 3 months or more, regardless of cause [2]. Kidney failure is defined as either (a) GFR less than 15 ml/min/ 1.73 m^2, which is accompanied in most cases by signs and symptoms of uremia, or (b) a need to start kidney replacement therapy (dialysis or transplantation) [3].

The most common causes of CKD are diabetes mellitus, hypertension, and glomerulonephritis. Together, these comprise ~75% of all adult cases [4]. The major outcomes of CKD, regardless of cause, include progression to kidney failure, complications of decreased kidney function, and cardiovascular disease. Increasing evidence indicates that some of these adverse outcomes can be prevented or delayed by early detection and treatment [5].

Chemerin, also known as tazarotene-induced gene 2 (TIG2) and retinoic acid receptor responder 2 (RARRES2), is a newly discovered adipokine highly expressed by a number of tissues and organs including adipose tissue, liver, pancreas, lung, and skeletal muscles [6].

Several specific functions have been related to chemerin so far, including regulation of specific immune cell migration [7,8], regulation of adipogenesis [9], and anti-inflammatory effects on macrophages [10]. Chemerin is secreted as an 18-kDa inactive proprotein formed of 143 amino acids, termed as prochemerin [11].

Enzymes that contribute to activation of chemerin and promote the conversion of inactive prochemerin into the active form chemerin include serine proteases of the

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coagulation, fibrinolytic, and inflammatory cascades, circulating carboxypeptidases, as well as staphopain B, a cysteine protease secreted by *Staphylococcus aureus*, which is found in some pathological conditions [11].

Prochemerin, the inactive form of chemerin, can be converted to chemerin by either serine proteases or cysteine proteases. Serine proteases result in the production of stimulatory chemerin, whereas cysteine proteases result in the production of inhibitory chemerin, termed as inhibitory peptide chemerin 15 [12].

Chemerin has different roles at the physiological level. The main role of chemerin has been proven to be related to the adipose tissue. Chemerin can enhance insulin sensitivity of adipocytes by stimulating the process of glucose transport through different tissues [13].

The metabolic associations of an elevated circulating chemerin level in the context of uremia demonstrate that high chemerin levels predict a better survival in CKD patients. Furthermore, associations between circulating chemerin levels and GFR, insulin resistance, blood lipids and inflammatory markers, but not with body fat, have been reported [14]. A study has reported circulating chemerin in a CKD population, finding increased levels in hemodialysis patients, as well as an inverse correlation with residual renal function [15]. However, as links between circulating chemerin and inflammation, body composition, and metabolism were not investigated, they explored these associations, as well as the possibility that chemerin predicted 5-year mortality in an observational cohort study of incident dialysis patients.

The aim of the study was to find the role of serum chemerin in CKD patients.

Patients and methods

This study was conducted on 40 patients with CKD and 22 apparently healthy participants serving as the control group. All patients were selected from Internal Medicine Department, Al Zahraa University Hospital, and Nephrology Department Medical Insurance Hospital, Helwan in the period between December 2013 and March 2014.

Group I included 22 healthy participants as the control group (11 male and 11 female); their ages ranged between 22 and 65 years, with a mean age of 43±13.11 years.

Group II included 40 CKD patients (19 male and 21 female); their ages ranged between 18 and 62 years, with a mean age of 43±12.17 years. This group was further divided into two groups:
Group IIa included 20 patients with end-stage renal disease under regular hemodialysis (10 male and 10 female); their ages ranged between 18 and 60 years, with a mean age of 41.35±11.95 years.
Group IIb included 20 patients with renal impairment on conservative therapy who have not started hemodialysis yet (nine male and 11 female); their ages ranged between 19 and 62 years, with a mean age of 41.75±12.70 years.

Exclusion criteria

Patients with acute or chronic known infection, cardiovascular disease, hypertension, diabetes mellitus, chronic liver disease (hepatitis B or C), or HIV infection were excluded.

After taking a written consent from all participants participating in this study and approval of ethical committee of Faculty of Medicine, Al-Azhar University, they were subjected to the following tests:

(1) Full history and full clinical examination.
(2) Complete blood picture (CBC).
(3) Fasting blood glucose.
(4) Kidney function tests (serum urea and serum creatinine).
(5) Serum glutamic oxaloacetic transaminase (SGOT) and AGPT.
(6) Lipid profile [total cholesterol, triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL)].
(7) Serum insulin.
(8) Serum high-sensitivity C-reactive protein (hs-CRP).
(9) Serum chemerin.

Five milliliters of fasting (12–16 h) venous blood samples were taken from each subject in the study and divided into two parts: the first part was 2 ml of blood and was put in a tube containing EDTA for CBC determination on Coulter Counter T890 (Coulter Counter, Harpenden, UK). The second part was 3 ml of blood and was left to clot and the serum was separated by centrifugation for 15 min at 3000*g*. Samples should be assayed immediately after collection or they should be stored at −20°C for determination of fasting blood glucose (which is determined immediately on Hitachi 912 autoanalyzer using colorimetric techniques) and kidney function tests. SGOT, serum glutamic pyruvic transaminase (SGPT), lipid profile, insulin, and chemerin were also determined.

(1) The determination of serum urea, creatinine, SGOT, SGPT, total cholesterol, and TG was performed on Hitachi 912 auto analyzer (Roche Diagnostics GmbH, D-68298 Mannheim, USA) by colorimetric techniques. For determination of HDL-cholesterol, phosphotungestic acid and magnesium ions are used for precipitating all lipoproteins, except HDL fraction, which was present in the supernatant and measured by the autoanalyzer. LDL-cholesterol was measured by Friedwald formula [16].
(2) Fasting serum insulin was determined using radioimmunoassay [17]. Insulin resistance was calculated as HOMA-IR using the following equation [18]:

$$\text{HOMA} - \text{IR} = \frac{\text{Fasting glucose (mg/dl)} \times \text{fasting insulin (}\mu\text{IU/ml)}}{405}.$$

(3) Determination of hs-CRP was done by a solid-phase immunosorbent assay (enzyme-linked immunosorbent assay) [19], and the kit was supplied by DRG International Inc. (Springfield, New Jersey, USA).
(4) Human chemerin is determined by sandwich enzyme immunoassay [20], and the kit was supplied from bio Vendor (Bio Vendor GmbH, Heidelberg, Germany).

Statistical analysis

Data were collected, coded, revised, and entered to the Statistical Package for Social Science version 20 (IBM SPSS version 20, USA). The qualitative data were presented as number and percentages and as mean, SD, and ranges with the quantitative data. Comparison between groups with qualitative data was done by using χ^2-test, whereas the comparison between two groups with quantitative data was done by independent *t*-test; more than two groups were compared using one-way analysis of variance followed by post-hoc least significant difference test when the comparison showed significant difference. Spearman's correlation coefficients were used to assess the relation between two quantitative parameters in the same group. Receiver operating characteristic curve was used to assess the best cutoff point with its sensitivity, specificity, positive predictive value, and negative predictive value.

Results

Table 1 shows a comparison between control group I and patient group II regarding age, sex, and BMI, and there was no statistically significant difference between patient and control groups regarding age and sex. In addition, there was a high statistically significant difference in BMI between the patient and control groups.

Table 2 shows a comparison between control group I and whole patient group II, with a highly statistically significant difference in mean serum urea, mean serum creatinine, mean serum HDL, mean serum LDL, mean serum TG, mean serum SGOT, mean serum insulin, and HOMA index and CBC in the patient group in comparison with the control group. It also shows a statistically significant difference in cholesterol in the patient group in comparison with the control group.

Table 3 shows a highly statistically significant difference in mean serum chemerin and mean serum hs-CRP in the patient group in comparison with the control group.

Table 4 reveals a nonsignificant difference between the three groups regarding age and sex. In addition, there was a highly significant increase in BMI in both patient groups compared with the control group.

Table 5 shows a highly statistically significant difference between control group I, under hemodialysis group IIa, and renal impairment group IIb in CBC, mean serum urea, mean serum creatinine, mean serum SGPT,

Table 1 Comparison between control group I and patient group II regarding age, sex, and BMI

	Control group [*n* (%)]	Patient group [*n* (%)]	χ^2-Test	
			χ^2	*P*-value
Sex				
Female	11 (50.0)	21 (52.5)	0.036	0.851
Male	11 (50.0)	19 (47.5)		
Age				
Mean±SD	43.23±13.11	41.55±12.17	0.505	0.615
Range	22–65	18–62		
BMI				
Mean±SD	19.5±4.33	26.14±3.6	0.154	0.000
Range	18–26	19.04–41.4		

$P>0.05$, NS. $P<0.05$, S. $P<0.01$, HS.

Table 2 Comparison between patients and control group regarding different laboratory parameters

	Control group	Patient group	Independent *t*-test	
	Mean±SD	Mean±SD	*t*	*P*-value
WBCs	5.76±0.81	6.87±1.92	–2.599	0.012
RBCs	4.11±0.34	3.61±1.00	2.272	0.027
Hb	12.10±0.73	9.90±1.91	5.169	0.000
Urea	18.50±4.07	121.63±48.16	–9.988	0.000
Creatinine	0.87±0.20	5.51±3.65	–5.940	0.000
SGPT	15.09±4.32	16.16±8.08	–0.574	0.568
SGOT	21.41±3.14	16.70±9.07	2.352	0.022
Cholesterol	154.18±21.88	181.03±52.34	–2.291	0.025
TG	90.68±16.62	115.58±39.15	–2.837	0.006
HDL	105.86±11.87	43.85±14.05	17.533	0.000
LDL	51.77±6.81	126.83±18.78	–18.050	0.000
FBG	94.73±11.31	94.93±13.93	–0.056	0.956
FSI	9.30±1.76	15.87±3.07	–9.218	0.000
HOMA index	2.20±0.49	3.72±0.87	7.677	0.000

HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBC, red blood cell; TG, triglyceride; WBC, white blood cell.

Table 3 Comparison between control group I and patient group II regarding serum chemerin and serum high-sensitivity C-reactive protein

	Control group	Patient group	Independent *t*-test	
	Mean±SD	Mean±SD	*t*	*P*-value
Chemerin	121.35±18.82	290.29±98.18	–7.962	0.000
hs-CRP	4.65±1.82	15.23±7.11	–6.839	0.000

hs-CRP, high-sensitivity C-reactive protein.

Table 4 Comparison between the three studied groups control I, under hemodialysis IIa, and renal impairment IIb groups regarding age, sex, and BMI

	Control group I [*n* (%)]	Under hemodialysis IIa [*n* (%)]	Renal impairment IIb [*n* (%)]	χ^2-Test	
				χ^2	*P*-value
Sex					
Female	11 (50.00)	10 (50.00)	11 (55.00)	0.136	0.934
Male	11 (50.00)	10 (50.00)	9 (45.00)		
Age					
Mean±SD	43.23±13.11	41.35±11.95	41.75±12.70	0.131	0.878
Range	22–65	18–60	19–62		
BMI					
Mean±SD	19.50±4.33	26.12±4.87	26.18±1.84	20.368	0.000
Range	18–26	19.04–41.4	23.2–30		

and mean serum SGOT. There was a highly statistically significant difference between control group I, under hemodialysis IIa, and renal impairment IIb in mean serum concentrations of cholesterol, TG, HDL, LDL, fasting serum insulin (FSI), and mean HOMA. However, there was no statistically significant difference between control group, under hemodialysis group, and renal impairment group in mean fasting blood glucose (FBG).

Table 6 reveals that comparisons between the control group I and both patient groups and between the two patient groups showed highly statistically significant difference in CBC, mean serum urea, and mean serum creatinine ($P<0.01$), and a statistically significance in mean serum SGPT when comparing the control group with group IIa ($P<0.05$). The comparison between the control group I and renal impairment IIb group showed a highly statistically significant difference in mean serum urea and mean serum creatinine ($P<0.01$). Post-hoc analysis for laboratory parameters among the three studied groups: The comparison between the control group versus the under hemodialysis group showed a high statistical significance in TG, HDL, LDL, FSI, and HOMA index ($P<0.01$). The comparison between the control group versus renal impairment group showed high statistical significance in cholesterol, HDL, LDL, FSI, and HOMA index ($P<0.01$). The comparison between the patients under hemodialysis versus renal

Table 5 Comparison between the three studied groups, control I, under hemodialysis IIa, and renal impairment IIb groups, regarding laboratory data

	Control group I	Under hemodialysis IIa	Renal Impairment IIb	One-way ANOVA	
	Mean±SD	Mean±SD	Mean±SD	*F*	*P*-value
WBCs	5.76±0.81	7.75±2.20	6.00±1.05	11.260	0.000
RBCs	4.11±0.34	3.18±1.20	4.04±0.45	9.554	0.000
Hb	12.10±0.73	8.60±1.76	11.20±0.92	46.930	0.000
Urea	18.50±4.07	142.60±48.16	100.65±38.92	67.930	0.000
Creatinine	0.87±0.20	7.19±3.35	3.84±3.18	30.295	0.000
SGPT	15.09±4.32	12.52±4.62	19.80±9.20	6.705	0.002
SGOT	21.41±3.14	12.65±5.74	20.75±10.07	10.378	0.000
Cholesterol	154.18±21.88	151.70±54.58	210.35±28.87	15.957	0.000
TG	90.68±16.62	134.20±35.76	96.95±33.73	12.935	0.000
HDL	105.86±11.87	49.60±16.02	38.10±8.86	176.745	0.000
LDL	51.77±6.81	121.57±16.57	132.08±19.78	175.546	0.000
FBG	94.73±11.31	95.48±9.50	94.37±17.53	0.037	0.964
FSI	9.30±1.76	16.37±3.55	15.37±2.49	43.452	0.000
HOMA index	2.18±0.48	3.85±0.89	3.57±0.84	30.281	0.000

ANOVA, analysis of variance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RBC, red blood cell; TG, triglyceride; WBC, white blood cell.

Table 6 Post-hoc analysis for the laboratory data between the three studied groups

Parameters	Post-hoc analysis: LSD test		
	Control vs. under hemodialysis	Control vs. renal impairment	Under hemodialysis vs. renal impairment
WBCs	0.000	0.595	0.000
RBCs	0.000	0.767	0.001
Hb	0.000	0.020	0.000
Urea	0.000	0.000	0.000
Creatinine	0.000	0.001	0.000
SGPT	0.046	0.243	0.403
SGOT	0.000	0.756	0.000
Cholesterol	0.831	0.000	0.000
TG	0.000	0.496	0.000
HDL	0.000	0.000	0.000
LDL	0.000	0.000	0.033
FSI	0.000	0.000	0.244
HOMA index	0.000	0.000	0.256

HDL, high-density lipoprotein; LDL, low-density lipoprotein; LSD, least significant disease; RBC, red blood cell; TG, triglyceride; WBC, white blood cell.

Table 7 Comparison between the three studied groups regarding serum chemerin and serum high-sensitivity C-reactive protein

	Control group	Under hemodialysis	Renal impairment	One-way ANOVA	
	Mean±SD	Mean±SD	Mean±SD	*F*	*P*-value
Chemerin	121.35±18.82	373.55±55.14	207.03±46.40	189.703	0.000
hs-CRP	4.65±1.82	20.76±5.79	9.70±2.38	101.764	0.000

ANOVA, analysis of variance; hs-CRP, high-sensitivity C-reactive protein.

impairment patients showed high statistical significance in cholesterol, TG, and HDL ($P<0.01$). It also showed a statistical significance in LDL ($P<0.05$).

Table 7 shows a comparison between the three studied groups regarding mean serum chemerin and mean serum hs-CRP. There was a high statistically significant difference between the control group, under hemodialysis group, and renal impairment group in serum chemerin and serum hs-CRP.

Table 8 shows a post-hoc analysis for serum chemerin and serum hs-CRP among three studied groups, which show a highly statistical significance on both studied parameters ($P<0.01$).

Table 9 demonstrates the correlation between serum chemerin and studied parameters in the under hemodialysis group, renal impairment group, and in all patients' group; there was a significant positive correlation between chemerin and urea, creatinine, FSI, HOMA index, and hs-CRP

Table 8 Post-hoc analysis for serum chemerin and serum high-sensitivity C-reactive protein among the three studied groups

Parameters	Post-hoc analysis: LSD test		
	Control vs. under hemodialysis	Control vs. renal impairment	Under hemodialysis vs. renal impairment
Chemerin	0.000	0.000	0.000
hs-CRP	0.000	0.000	0.000

hs-CRP, high-sensitivity C-reactive protein; LSD, least significant difference.

Table 9 Correlation between chemerin and the studied parameters in under hemodialysis group, renal impairment group, and in all patients group

Parameters	Chemerin					
	Under hemodialysis		Renal impairment		All patients	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value
Age	0.079	0.741	–0.074	0.755	–0.027	0.868
BMI	–0.002	0.992	–0.211	0.373	–0.123	0.451
WBCs	0.313	0.179	–0.147	0.536	0.405**	0.010
RBCs	0.107	0.652	–0.265	0.259	–0.516**	0.001
Hb	–0.026	0.912	–0.334	0.150	–0.653**	0.000
Urea	0.836**	0.000	0.358	0.121	0.677**	0.000
Creatinine	0.999**	0.000	0.995**	0.000	0.918**	0.000
SGPT	0.403	0.078	–0.149	0.531	–0.366*	0.020
SGOT	0.167	0.481	0.171	0.471	–0.330*	0.038
Cholesterol	0.017	0.944	–0.208	0.380	–0.619**	0.000
TG	0.422	0.064	–0.143	0.547	0.530**	0.000
HDL	0.176	0.457	–0.204	0.388	0.376*	0.017
LDL	–0.167	0.481	–0.259	0.271	–0.313*	0.049
FBG	–0.124	0.602	–0.108	0.651	–0.013	0.937
FSI	0.995**	0.000	0.967**	0.000	0.591**	0.000
HOMA index	0.848**	0.000	0.526*	0.017	0.440**	0.004
hs-CRP	0.992**	0.000	0.983**	0.000	0.994**	0.000

HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; LSD, least significant disease; RBC, red blood cell; TG, triglyceride; WBC, white blood cell. *Significance. **Highly significance.

among the hemodialysis patients ($P<0.01$). In addition, there was a positive correlation between serum chemerin and creatinine, FSI, HOMA index, and hs-CRP in renal impairment patients ($P<0.01$). There was also a correlation between chemerin and white blood cells, red blood cells (RBCs), Hb, urea, creatinine, cholesterol, TG, LDL, HDL, FBG, FSI, SGOT, SGPT, and hs-CRP in all patients' group ($P<0.01$).

Table 10 and Fig. 1 shows that serum chemerin level is considered to have better positive predictive value, sensitivity, and specificity.

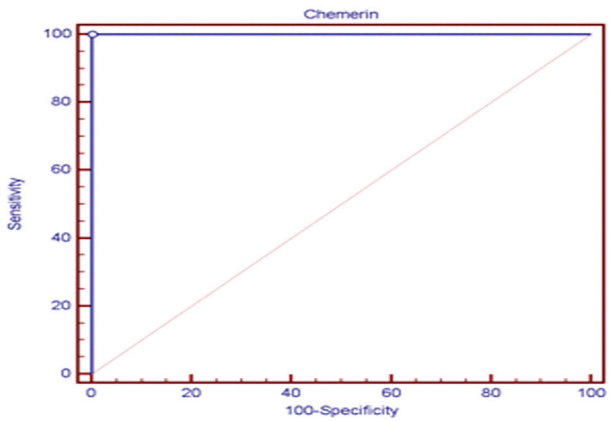
Table 11 and Fig. 2 show that chemerin level is considered to have a better positive predictive value, sensitivity, and slightly better specificity.

Table 10 Receiver operating characteristic curve between patients and controls regarding serum chemerin

Cut off point	AUC	Sensitivity	Specificity	PPV	NPV
>147.5	100.0	100.00	100.00	100.0	100.0

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

Figure 1



Receiver operating characteristic (ROC) curve analysis between patients under hemodialysis and patients with renal impairment regarding serum chemerin.

Discussion

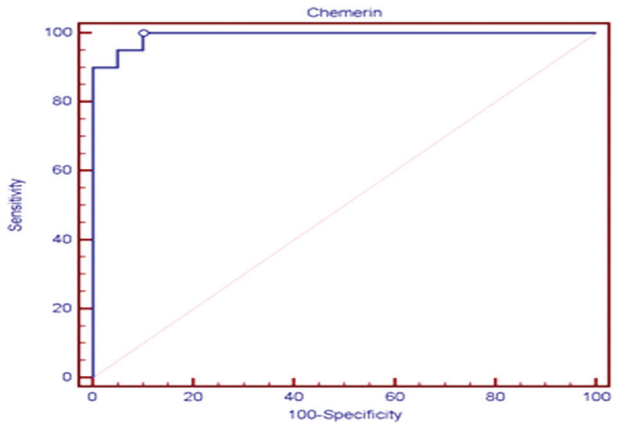
We aimed in the present work to study serum chemerin levels and to determine their relation to patients with CKD.

Table 11 Receiver operating characteristic curve between patients under hemodialysis and patients with renal impairment regarding serum chemerin

Cut off point	AUC	Sensitivity	Specificity	PPV	NPV
274.9	99.2	100.0	90.0	90.9	100.0

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

Figure 2



Receiver operating characteristic (ROC) curve between patients under hemodialysis and patients with renal impairment regarding serum chemerin.

In this study, we compared three studied groups as regards age, sex, and BMI, and we found no significant difference in both age and sex, but we found a significant increase in BMI in patients more than the control group, which may be because of the increase in water loading and obesity in the diseased group, which was in contrast to the study by Dorte *et al.* [21], who showed that CKD patients had a significantly lower BMI compared with control patients, which results from the environmental and ethnic difference.

In our study, we found a statistical significance as regards Hb concentration, white blood cells, RBCs, FBG, FSI, and HOMA index between the control group and the patient groups. This was found also by Kilpatrick *et al.* [22] and Dorte *et al.* [21].

The studies found that patients in the renal impairment group and under hemodialysis group had anemia due to decreased erythropoietin (the most important factor), iron deficiency, folate deficiency, hemolysis, and bone marrow fibrosis because of the shortened life span of RBCs.

As regards lipid profile (cholesterol, TGs, HDL, LDL), there were significant differences between the control group and patient group, which was in agreement with Kilpatrick *et al.* [22] and Dorte *et al.* [21]. Dysregulation of lipid metabolism in the patient group can contribute to atherogenic diathesis and possibly to progression of renal disease and impaired energy metabolism in CRF. Hyperlipidemia can potentially accelerate progression of renal disease by several mechanisms. First, reabsorption of fatty acids, phospholipids, and cholesterol contained in the filtered proteins (albumin and lipoproteins) by tubular epithelial cells can stimulate tubulointerstitial inflammation, foam cell formation, and tissue injury. Second, accumulation of lipoproteins in glomerular mesangium can promote matrix production and glomerulosclerosis [23].

In this study, we found that chemerin level was significantly higher among patients in the under hemodialysis group compared with the other two groups. This was supported by Dörte *et al.* [21] and Fouque *et al.* [24], who reported that chemerin was more than two-fold higher in CKD patients compared with the control group. Studies found that elevated serum chemerin levels may be a consequence of impaired kidney in patients. Impaired clearance or catabolism of chemerin in kidney may lead to the accumulation of chemerin in the blood. This suggests that elevated serum chemerin levels are significantly associated with serum creatinine and urea in renal impairment and under hemodialysis patients. In our study, we found that chemerin level was significantly higher among the under hemodialysis patient group compared with renal impairment patient group because the serum urea and creatinine were higher in the under hemodialysis patient group compared with the renal impairment patient group, as the sample from the under hemodialysis patient group was collected before dialysis.

In our study, there is a significant positive correlation between chemerin level versus serum creatinine and urea. Dörte *et al.* [21] and Pfau *et al.* [15] support the same result which that referred to infiltration of kidney glomeruli by inflammatory cell like monocyte and macrophage result in glomerular injury and tubule-interstitial damage that decrease the functional capability of kidney to excrete waste products. Another explanation was obtained by the Pfau *et al.* [15,] who postulated that impaired kidney function by over-production and impaired degradation of extracellular matrix components leads to their accumulation in basement membrane and mesangial region in glomerulus or may be because of the presence of hyperglycemia, glomerular hypertension, advanced glycation end products, and activation of polyol pathway [15].

In our study, there is a significant positive correlation between chemerin level and cholesterol, TG, HDL,

and LDL This was supported by Xu *et al*. [25], who reported that chemerin is a proinflammatory cytokine activating immune cells, and it might play a role in the inflammation of adipose tissue that occurs in obesity.

In addition, in our study, there is a positive significant correlation between chemerin level concentrations and FBG, FSI, and HOMA-IR index in the CKD group patients. This result agrees with Sell and Eckel [6]; Dorte *et al*. [21]; Lehrke *et al*. [26]; and Weigert *et al*. [27]. Sell and Eckel attributed this to the fact that chemerin induces insulin resistance in peripheral tissue such as skeletal muscle and inhibits glucose uptake. Another explanation was obtained by Weigert *et al*. [27], who postulated that, in adipocytes, chemerin has the opposite effect, where it increases insulin-stimulated glucose uptake, and in turn stimulates insulin sensitivity. Hence, the increase in the level of circulating chemerin is a compensatory metabolism in patient with insulin resistance.

In our study, there is a positive correlation between chemerin concentration levels and hs-CRP index in end-stage renal disease patients. This was in agreement with the study by Bozaoglu *et al*. [14], who suggested that chemerin is a chemotactic agent that was recently identified as the ligand of ChemR23, a serpentine receptor expressed by activated macrophages and monocyte-derived dendritic cells, as previously mentioned. This fact suggests a key role of the ChemR23/chemerin axis in directing plasmacytoid dendritic cell trafficking, which can play a significant role in regulating the immune response by enhancing chemoattraction of the cells of the immune response toward sites of pathological inflammation.

The diagnostic performance of serum chemerin in detecting patients with renal impairment and under hemodialysis and control healthy persons revealed that the best cutoff level for chemerin in patient groups was greater than 147.5 ng/ml, with a diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, and efficiency of 100, 100, 100, and 100%, respectively, and an area under the curve of 100.

The diagnostic performance of serum chemerin in detecting patients with renal impairment and under hemodialysis reveals that the best cutoff level for chemerin was 249 ng/ml, with a diagnostic sensitivity, diagnostic specificity, positive predictive value, negative predictive value, and efficiency of 100, 90, 90.9, and 100%, respectively, and an AUC of 99.2.

An association of chemerin serum levels with metabolic syndrome-related parameters, including BMI [28], fasting insulin (FI), TGs [29], HDL-cholesterol [28], leptin [29], and C.reactive protein (CRP) [28], has been shown. In agreement with these findings, chemerin is positively correlated with BMI, FI, and CRP, whereas GFR remains independently associated with circulating chemerin. Interestingly, GFR also independently predicts chemerin serum levels in the CKD patients, which indicates that renal function is a significant predictor of circulating chemerin not only in subjects with (near) normal glomerular filtration but also in patients with end-stage renal disease.

Conclusion

We found a significantly higher chemerin level in patients with impaired kidney function compared with normal control group and much increase in patients under hemodialysis compared with the other two groups.

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Conflicts of interest

There are no conflicts of interest.

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