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Evaluation of galectin-3 and other biochemical parameters in chronic kidney disease patients on hemodialysis in Erbil city

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Abstract

Background and objective: Chronic kidney disease represents a leading cause of death in many countries. End-stage renal disease is the final stage of chronic kidney disease, in which the kidneys are no longer function well enough for the patient to live without renal replacement therapy. Galectin-3 is a soluble beta-galactoside-binding lectin protein involved in the fibrosis of many solid organs, including the heart and kidney. This study aimed to evaluate galectin-3 and other biochemical parameters in hemodialysis patients.

Methods: The design is a cross-sectional study with a comparison group. A total of 70 chronic kidney disease patients on regular hemodialysis from Erbil Dialysis Center in Erbil City and 68 healthy subjects were enrolled. The serum levels of galectin-3 were determined by enzyme-linked immunosorbent assay method.

Results: The mean level of serum galectin-3 was non-significantly higher in hemodialysis patients compared to the control group (P = 0.594). However, the serum level of galectin-3 was significantly higher in hemodialysis patients with cardiovascular disease compared to hemodialysis patients without cardiovascular disease (P = 0.0220). Serum galectin-3 level was significantly higher in hemodialysis patients aged 36-50 and 51-70 years old compared to hemodialysis patients aged 20-35 years old (P = 0.013, P = 0.026), respectively.

Conclusion: Serum galectin-3 might be used as a biomarker for hemodialysis patients with cardiovascular disease.

Keywords: Galectin-3; Chronic kidney disease; Hemodialysis.

Introduction

Chronic kidney disease (CKD) is a major non-communicable disease with an increasing prevalence over the past few years.[1] CKD has an important effect on both the population level, by increasing healthcare costs and the demand for healthcare services, and also affects the patient by decreasing life expectancy and quality of life.[2] In a recent systematic review and meta-analysis, the global prevalence of all five stages of CKD was estimated to be 13.4%.[3] Based on Kidney Disease Improving Global Outcomes (KDIGO) guidelines chronic kidney disease is defined by the presence of abnormality in the structure or function of the kidneys for >3 months, with implications for health.[4] Diabetes mellitus and hypertension are the leading risk factors for CKD.[5] Cardiovascular diseases (CVD) is present in greater than 50% of dialysis patients, and the relative risk of death due to CVD events in hemodialysis patients is reported to be twenty times higher than in the general population.[6]

There are five stages of chronic renal failure (CRF) based on the glomerular filtration rate, stage five of CRF is also called end-stage renal disease (ESRD), in this stage glomerular filtration rate (GFR) is less than 15ml/min/1.73m^2 and dialysis is

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preferred at this stage.[7] ESRD is the final stage of chronic kidney disease, and is defined as an irreversible decline in a person's kidney function that is severe, enough to be fatal in the absence of dialysis or transplantation.[8] Because of its gradually growing morbidity, high mortality, and high health care expenditures, ESRD is a major clinical and public health issue.[9] Hemodialysis (HD) is the commonest form of kidney replacement therapy (KRT) in the world.[10]

Human Galectin-3 (Gal-3) is a 35-kDa protein that is coded by a single gene (LGALS3), located on chromosome fourteen.[11] Galectin-3 participates in a variety of pathophysiological processes including, adhesion, proliferation, differentiation, apoptosis, and induction of inflammatory condition and fibrotic process.[12] Previous researches suggest that a higher concentration of galectin-3 may be related to the development of fibrosis of solid organ tissues, including the kidney, heart, and liver.[9] This study aimed to evaluate galectin-3 and other biochemical parameters in chronic kidney disease patients on hemodialysis.

Methods

Design of the study

A cross-sectional study with a comparison group.

Setting of the study

The study was conducted in both Erbil Dialysis Center in Erbil city and Rizgary Teaching Hospital.

Duration of the study

The study was conducted from October 2021 to April 2022.

Subjects of the study

A total of 138 adults participated in the study which was divided into two groups: 70 patients with chronic kidney failure on hemodialysis for greater than 3 months from Erbil Dialysis Center in Erbil city were selected as a case group and during the period of the study the researcher selected 68 subjects without kidney disease as a control group from Rizgary Teaching Hospital.

Sample collection and analysis

Five milliliters of vinous blood were withdrawn from 70 hemodialysis patients in Erbil Dialysis Center in Erbil city; pre-dialysis samples were taken before the administration of heparin. Also, five milliliters of venous blood were taken from 68 healthy participants. The blood that was taken from each participant was placed in yellow gel tubes. Clotted blood was centrifuged at (3000 rpm for 15 min). Apart from the serum of pre-hemodialysis patients and healthy participants were placed in 1,5ml eppendorf tubes and stored at -20°C for determination of serum galectin-3. Galectin-3 was analyzed with the enzyme-linked immunosorbent assay (ELISA) method. Human galectin-3 ELISA kit was used. The assay range was 0.156-10ng/ml. The other part of serum was used for evaluation of several biochemical assays which included serum creatinine and serum urea. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation was used for calculation of estimated glomerular filtration rate(eGFR).[13]

Ethical consideration

The research protocol was reviewed and approved by the ethical committee of the College of Health Sciences/ Hawler Medical University. A complete explanation of the nature and aim of the study was given to each participant, and they were reassured about the confidentiality of the data and their anonymity. In addition, their rights to refuse or participate in the present study were confirmed, and then oral informed consent was obtained for the interview.

Statistical Analysis

All statistical data were analyzed using Statistical Package for Social Sciences (SPSS, version 24) and GraphPad Prism9. The continuous variables were tested for normal distribution by Shapiro-Wilk test and presented as mean ± standard error of the mean (SEM) or median with interquartile ranges (IQR). Categorical

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variables presented as the number and percentage. The Chi-square test was used to show the significance of association between categorical variables. Comparisons between two independent groups were performed using the unpaired t test or Mann-Whitney test, while measurement data among multiple groups were done using one-way ANOVA followed by multiple comparison Tukey test or Kruskal–Wallis followed by Dunn's test. *P* ≤0.05 was considered statistically significant.

Results

Table 1 shows the socio-demographic characteristics of both hemodialysis (HD) patients and control groups. This study included 70 HD patients and 68 control subjects. The nearly matched criteria between the two groups were age and gender. Most of the HD patients were 51-70 years old (55.7%) and males (52.9%). Also, most of the control subjects were 51-70 years old (54.4%) and male (52.9%). The mean age ± standard error of the mean (SEM) for the HD patients was 50.30±1.679 years, and that of the controls was 49.75±1.699 years (*P* value = 0.818). Regarding marital status the highest percentage of both HD patients (58.6%) and controls (86.8%) were married and there was highly significant difference in marital status between HD patients and the control group (*P* value = 0.001). The majority of both HD patients (58.6%) and control groups (47.1%) were from urban areas. The result also shows that body mass index (BMI) was non-significantly (*P* value = 0.313) lower in HD patients compared to the control group, and the mean±SEM was 26.28±0.711 and 27.24±0.621, respectively.

Table 1 Baseline socio-demographic characteristics of hemodialysis patients and controls

Characteristics	HD Patients (n=70)	Control (n=68)	*P* value
Age/Years (Mean ± SEM)	50.30 ±1.679	49.75 ±1.699	0.818
Age group, n (%)			
20-35	14 (20%)	14 (20.6%)	
36-50	17 (24.3%)	17 (25.0%)	0.988
51-70	39 (55.7 %)	37 (54.4%)	
Body mass index kg/m^2 (Mean ± SEM)	26.28± 0.711	27.24± 0.621	0.313
Gender, n (%)			
Male	37 (52.9%)	36 (52.9%)	0.992
Female	33 (47.1%)	32(47.1%)	
Residency, n (%)			
Urban	41 (58.6%)	32 (47.1%)	
Suburban	14 (20.0%)	21 (30.9%)	0.289
Rural	15 (21.4%)	15 (22.1%)	
Marital Status, n (%)			
Single	15 (21.4%)	5 (7.4%)	
Married	41 (58.6%)	59 (86.8%)	0.001
Widowed/widower	14 (20.0 %)	4 (5.9%)	

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Table 2 shows the clinical characteristics of hemodialysis patients. Regarding chronic diseases, 81.4%, 45.7% and 28.6% of hemodialysis patients had hypertension, cardiovascular disease, and diabetes mellitus, respectively. There was a statistically significant difference between hemodialysis patients with and without hypertension (P = 0.030), and also there was a significant difference between hemodialysis patients with and without diabetes mellitus (P value = 0.001). A highly significant difference between hemodialysis patients with and without cardiovascular disease (P = 0.000) was recorded. Concerning the duration of hemodialysis treatment, 70.0% of patients received hemodialysis treatment for 1-5 years.

As shown in Table 3, the serum creatinine level was significantly (P <0.001) higher in HD patients compared to the control group, and the mean±SEM was 8.097±0.314 and 0.651±0.023, respectively. Also, the serum urea level was significantly (P <0.001) higher in HD patients compared to the control group, and the mean±SEM was 132.5±5.406 and 25.29±0.886, respectively. The result also shows that the estimated glomerular filtration rate (eGFR) was significantly (P <0.001) lower in HD patients compared to the control group, and the mean±SEM was 7.871±0.542 and 111.8±1.657, respectively. Regarding galectin-3, the serum galectin-3 level was non-significantly (P = 0.594) higher in HD patients compared to the control group, and the mean±SEM was 1.037±0.169 and 0.941±0.055, respectively.

Table 2 Clinical characteristics of hemodialysis patients

Variables	Hemodialysis patients (n=70)	*P* value
Hypertension, n (%)		
Yes	57 (81.4%)	0.030
No	13 (18.6%)	
Diabetes mellitus, n (%)		
Yes	20 (28.6)	0.001
No	50 (71.4)	
Cardiovascular disease, n (%)		
Yes	32 (45.7%)	0.000
No	38 (54.3%)	
Duration of hemodialysis treatment, n (%)		
<1 Year	5 (7.1%)	
1-5 Years	49 (70%)	
>5 Year	16 (22.9%)	

Table 3 Comparison of studied parameters between hemodialysis patients and control subjects

Groups Parameters	Control (n=68)	HD-patients (n=70)	*P* value
Creatinine (mg/dL)	0.651 ± 0.023	8.097± 0.314	**<0.001**
Urea (mg/dL)	25.29±0.886	132.5±5.406	**<0.001**
eGFR (ml/min/1.73m^2)	111.8±1.657	7.871±0.542	**<0.001**
Galectin-3 (ng/ml)	0.941±0.055	1.037±0.169	0.594

The result expressed as mean± standard error of the mean. Unpaired t test was used.

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Table 4 shows the comparison of the median (interquartile range) or mean± standard error of the mean of numerical variables in different age groups of hemodialysis patients. (A) Indicate hemodialysis patients whose ages were 20 -35 years old, (B) indicate hemodialysis patients whose ages were 36-50 years old, and (C) indicate hemodialysis patients whose ages were 51-70 years old.

As shown in Table 4, the serum galectin-3 level was significantly (P = 0.013) higher in group (B) compared to group (A) and the median (interquartile range) was 0.832 (0.562-1.210) ng/ml and 0.477 (0.410-0.705) ng/ml, respectively. Also, serum galectin-3 level was significantly (P = 0.026) higher in group (C) compared to group (A) and the median (interquartile range) was 0.772 (0.577-0.903) ng/ml and 0.477 (0.410-0.705) ng/ml, respectively. Serum urea level was significantly (P = 0.008) higher in group (C) compared to group (B), and the mean±SEM was 146.1±7.194 and 108.0±11.23, respectively. Body mass index (BMI) was significantly (P = 0.0014) higher in group (B) compared to group (A) and the median (interquartile range) was 27.00 (25.15-32.15) and 20.25 (17.85-22.45), respectively. Also, BMI was significantly (P = 0.0017) higher in group (C) compared to group (A), and the median (interquartile range) was 27.20 (23.10-30.40) and 20.25 (17.85-22.45), respectively.

Figure1 illustrates the comparison between serum levels of galectin-3 in hemodialysis (HD) patients with and without cardiovascular disease (CVD). The serum galectin-3 level was significantly (P = 0.0220) higher in HD patients with CVD (n=32) compared to HD patients without CVD (n=38), and the median (interquartile range) was 0.822 (0.589-1.139) ng/ml and 0.601 (0.477-0.888) ng/ml, respectively.

Table 4 Median (interquartile range) or mean±standard error of mean of numerical variables in different age groups of hemodialysis patients

Age Groups Parameters	20-35 (n=14) (A)	36-50 (n=17) (B)	51-70 (n=39) (C)
Galectin-3, (ng/ml)	0.477 (0.410-0.705)	0.477 (0.410-0.705)	0.772 (0.577-0.903)*
Creatinine, (mg/dL)	8.165 (6.538-11.68)	8.165 (6.538-11.68)	8.340 (7.520-9.720)
Urea, (mg/dL)	124.1±8.038	124.1±8.038	146.1±7.194##
eGFR,(ml/min/1.73m^2)	7.000 (4.750-9.500)	7.000 (4.750-9.500)	6.000 (5.000-7.000)
BMI, (kg/m^2)	20.25 (17.85-22.45)	20.25 (17.85-22.45)	27.20 (23.10-30.40)**

* or ** Indicates the significance comparison between B and C age with A; ## indicates the significance comparison between B age with C age. *Refers to (P <0.05), ** or ## Refers to (P <0.01). One-way ANOVA test or Kruskal–Wallis test were used.

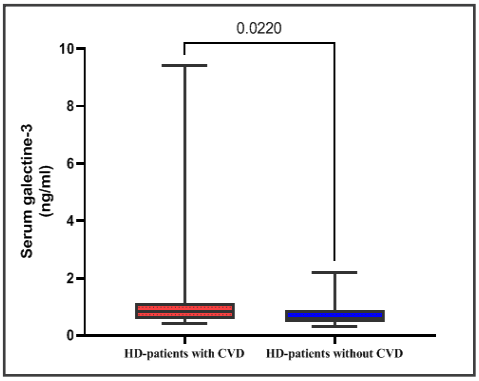

Figure 1 Comparison between serum galectin-3 levels in HD patients with and without CVD disease.

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Discussion

Globally, chronic kidney disease is a major contributor to morbidity and mortality.[14] End -stage renal disease (ESRD) is a rapidly increasing global health and health care burden.[15] Studies have demonstrated that the risk of chronic renal failure development rises with age, a study done in Erbil shows that the age of most hemodialysis patients was 51 and above (68.3%).[16] This finding is close to our results which revealed that the highest rate of hemodialysis patients was 51-70 (55.7%) years old.

A study conducted by Ali et al.[16] shows that most of the HD patients were males (51.5%) and live in urban areas (89.2%). This finding agrees with our results in that most of the HD patients were male (52.9%) and live in urban areas (58.6%). Regarding body mass index (BMI), a study conducted by Sultan et al.[14] in Pakistan, reveals that the mean value of BMI of HD patients was 24. This finding is in agreement with the current results as the mean value of BMI of HD patients was 26.28.

For patients with end-stage renal disease on hemodialysis, cardiovascular disease is the main cause of morbidity and mortality. Because end-stage renal disease is frequently caused by hypertension and diabetes mellitus, the increased cardiovascular disease risk in these patients has been thought to be due to these underlying diseases.[6] In maintenance hemodialysis patients; hypertension is a significant risk factor for CVD.[17] In our study most of the hemodialysis patients were hypertensive (81.4%) and the duration of HD treatment for most of the patients (70.0 %) was between 1-5 years, these findings are close to the prior study.[16]

The most common and widely used markers to evaluate renal functioning are blood urea nitrogen (BUN) and serum creatinine, increase urea and creatinine in the serum are good indicators of kidney dysfunction.[18]In the present study, the mean value of estimated glomerular filtration rate (eGFR) in HD patients was 7 .871ml/min/1.73m^2 and in healthy subjects was 111.8ml/min/1.73m^2, these results agree with the previous study.[19]

Galectin-3 is most commonly expressed by activated macrophages and is involved in a variety of pathological processes such as inflammation, fibrosis, and growth of the tumor.[9] In the present study, serum level of galectin-3 was non-significantly higher in HD patients compared to the control group. This result is in disagreement with the previous study in which plasma galectin-3 level was significantly higher in HD patients compared to the control group.[20] This may be due to the proper treatment and dialyzer machine which is now used for chronic kidney disease patients on hemodialysis in Erbil city. Since our study is the only recent study to compare serum levels of galectin-3 between HD patients and control groups, additional research is needed to confirm our results.

The main cause of mortality in chronic renal failure patients on hemodialysis is cardiovascular disease.[19] Most important mechanisms of atherosclerosis development that are stimulated by local or circulating galectin-3 are the amplification of cardiovascular system inflammatory conditions and the accumulation of lipids in macrophages.[12] Galectin-3 may be a promising marker for cardiovascular risk stratification in patients on HD.[9] This finding supports our results in which serum galectin-3 level was significantly higher in hemodialysis patients with cardiovascular disease compared to hemodialysis patients without cardiovascular disease (P = 0.0220).

A prior study on the general population found that galectin-3 increased with increasing age.[21] This finding supports our results in which serum galectin-3 level was significantly higher in hemodialysis patients aged 36-50 and 51-70 years old compared to hemodialysis patients aged 20-35 years old (P = 0.013, P = 0.026), respectively. High body mass index is a risk factor for end-stage renal disease and the prevalence of obesity among ESRD

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patients requiring dialysis is rising.[22] A study was conducted by Çelik et al.[23] shows that BMI in the elderly significantly higher than in adult hemodialysis patients (P = 0.028), this finding is in accordance with our results in which BMI was significantly higher in HD patients aged 36-50 and 51-70 years old compared to HD patients aged 20-35 years old (P = 0.0014, P = 0.0017), respectively.

Conclusion

Serum galectin-3 level was non-significantly higher in hemodialysis patients compared to the control group. Serum level of galectin-3 was significantly higher in hemodialysis patients with cardiovascular disease compared to hemodialysis patients without cardiovascular disease. The level of serum galectin-3 was significantly influenced by age in hemodialysis patients.

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Competing interests

The authors declare that they have no competing interests.

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