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MCP-1 and Vitamin D Profiles in ESRD on Hemodialysis: A Case-Control Study in Al-Basrah City

Haneen Husham Fadhil[1], Rana Dawood Salman[2], Jubran Khaleel Hasan[3]
[1,2,3]University of Basrah, Iraq

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ABSTRACT

Objective: *This study aimed to examine and compare serum levels of vitamin D and monocyte chemoattractant protein-1 (MCP-1) in patients with end-stage renal disease (ESRD) undergoing haemodialysis versus healthy individuals, and to evaluate their diagnostic potential as biomarkers.* ***Method:*** *An observational cross-sectional design was employed involving 30 ESRD patients receiving regular haemodialysis and 34 age- and sex-matched healthy controls. Serum levels of vitamin D, MCP-1, parathyroid hormone (PTH), urea, creatinine, estimated glomerular filtration rate (eGFR), and blood pressure were assessed.* ***Results:*** *ESRD patients showed significantly elevated levels of urea, creatinine, PTH, and MCP-1, and significantly lower eGFR and vitamin D levels compared to controls ($p<0.001$). ROC analysis revealed high diagnostic accuracy for PTH (AUC=0.946), with moderate-to-good performance for vitamin D (AUC=0.732) and MCP-1 (AUC=0.700).* ***Novelty:*** *This study contributes to the limited regional data by identifying the potential of vitamin D and MCP-1 as accessible clinical biomarkers for nutritional and inflammatory assessment in ESRD patients undergoing haemodialysis, emphasizing their role in early detection strategies and patient monitoring.*

INTRODUCTION

Chronic kidney disease (CKD) represents a considerable global health concern, impacting more than 800 million people globally. The epidemiology indicates rising prevalence and incidence rates, especially among older people and individuals with comorbidities like diabetes and hypertension. Chronic kidney disease (CKD) impacts roughly 10% of the worldwide population, exhibiting a prevalence of 13.4% for stages 1-5 and 10.6% for stages 3-5. The prevalence of chronic kidney disease (CKD) is significantly greater in low- and middle-income nations, where healthcare resources are constrained [1]. The global incidence of CKD has increased by 89% over the past 27 years, with significant regional variations.

The prevalence of renal failure in Iraq has increased over the last few years. In Iraq, without the Kurdistan region, kidney disease is the fourth among the top ten causes of death at 6.06 %, with 5.9% for males and 5.84% for females [2]. In 2040, it is expected to be the 5th leading cause of years of life lost; a variety of factors, including diabetes, hypertension, infection, reduced blood supply to the kidneys, obstruction of the urinary tract, and genetic alterations, cause CKD [3]. Vitamin D is a secosteroid synthesized from cholesterol that requires activation by 25-hydroxylation in the liver to form 25OHD, followed by 1α-hydroxylation in the kidney, producing the active hormone dihydroxy vitamin D (1,25(OH)2D). Nearly all biological functions of vitamin D are believed to be

facilitated by its active form, 1,25(OH)2D, mostly signaling via the intracellular vitamin D receptor (VDR) [4]. Vitamin D's significance in the metabolism of calcium, phosphorus, and parathyroid hormones, as well as in neuronal and immunological cell development, is well established. Vitamin D deficiency is a risk factor for infectious, autoimmune, neurological, and cardiovascular disorders, commonly observed in people with diabetes, osteoporosis, and cancer. Insufficient vitamin D levels are associated with elevated inflammatory markers, indicating a connection between vitamin D status and inflammation in end-stage renal disease (ESRD) [5].

Vitamin D deficiency is a common concern in patients with end-stage renal disease (ESRD), especially in those on maintenance haemodialysis. Studies reveal that a considerable percentage of these patients display deficient serum vitamin D levels, potentially aggravating numerous health issues. A study revealed that 36.1% of ESRD patients undergoing haemodialysis exhibited vitamin D levels below 20 ng/ml, signifying insufficiency [6].

MCP-1 is Chemokine ligand 2 (CCL2), the first member of the C-C chemokine family to be identified and is a strong monocyte chemotactic factor. This human CC chemokine is 13 kDa and includes 76 amino acids. With serum concentrations ranging from 135.6 to 543.5 pg/ml, it is produced by a variety of cell types, including endothelium, fibroblasts, epithelial, smooth muscle, mesangial, astrocytic, monocytic, and microglial cells, after being exposed to cytokines (IL-1b, TNF-a) [7-9]. MCP-1 is a crucial chemokine implicated in the inflammatory mechanisms associated with chronic kidney disease (CKD). Increased MCP-1 levels are found in the plasma and urine of CKD patients, corresponding with diminished kidney function, heightened albuminuria, and augmented interstitial macrophage infiltration, all linked to adverse clinical outcomes and the advancement of renal injury [10,11].

In CKD patients, higher plasma MCP-1 levels are associated with diminished kidney function and an increased risk of mortality, irrespective of traditional cardiovascular risk factors. MCP-1 has been demonstrated to predict all-cause. Mortality and atherosclerotic events in CKD populations, underscoring its significance beyond renal implications [11]. This observational cross-sectional study aims to evaluate and compare the serum levels of Monocyte Chemoattractant Protein-1 (MCP-1) and vitamin D in patients with End-Stage Renal Disease (ESRD) undergoing hemodialysis versus healthy control subjects in Al-Basrah city. It also seeks to investigate potential alterations in inflammatory and nutritional biomarkers associated with ESRD and their possible role in the disease's pathophysiology.

RESEARCH METHOD

This is an observational cross-sectional study that includes patients with end-stage renal failure on hemodialysis. This study was conducted in Basrah Teaching Hospital from January -2024 to April 2024. Demographic and laboratory data were collected. A total of 64 patients were included, of whom (n=30) ESRD patients on hemodialysis were classified and defined based on the National Kidney Foundation KDOQI definition for

chronic kidney disease [12]. Chronic hemodialysis patients were eligible to enter the study if they agreed to participate, and n=34 were a healthy control group, with median ages of (50.4 ± 10.9) and (41 ± 10.6), respectively. Verbal consent was obtained from all participants. The study protocols received approval from the ethics committees of the Basrah Teaching Hospital and the Basrah Dialysis Center. Blood pressure was measured for each group, and blood samples were drawn from the participants. The following biomarkers were obtained: urea, creatinine, vit D, PTH, and MCP-1. Also, eGFR has been calculated. The ELISA technique was used to measure serum MCP-1

Inclusion criteria

Patients aged 30 to 70, and both genders suffering from renal failure and hypertension, were involved in the study.

Exclusion criteria

Pregnant women, breastfeeding, smokers, thyroid dysfunction, Patients with a history of chronic liver disease, hepatitis type B and C, malignancy, rheumatoid arthritis, immunosuppressant agents, disease-modifying antirheumatic drugs (DMARDs), kidney transplantation, and stroke were excluded from participating in this study.

Statistical analysis

The data were expressed as means and medians. A t-test analysis (unpaired test) was conducted to compare continuous variables.

RESULT AND DISCUSSION

Results

Concerning urea, the disease group shows significantly higher urea levels as compared to the control group (117.5 ± 39 vs 20.6 ± 6.7, *p*-value <0.0001), as shown in (Table 1). Concerning creatinine, the disease group shows significantly higher creatinine levels as compared to the control group (7.5 ± 2.1 vs 0.8 ± 0.2, *p*-value <0.0001), as shown in (Table 1). Concerning the eGFR value, the disease group shows significantly lower eGFR levels as compared to the control group (8 ± 3.3 vs 106.1 ± 22.7, *p*-value <0.0001), as shown in (Table 1). Concerning systolic blood pressure (SBP) levels, the disease group shows significantly higher systolic values as compared to the control group (144.6 ± 16.5 vs 121.1 ± 3, *p*-value <0.0001), as shown in (Table 1). Concerning diastolic blood pressure (DBP) levels, the disease group shows significantly higher diastolic values as compared to the control group (86.3 ± 13.8 vs 80.7 ± 1.9, *p*-value 0.031), as shown in (Table 1). Concerning Vitamin D levels, the disease group shows significantly lower vitamin D values as compared to the control group. (30.4 ± 15.94 vs 34.6 ± 17.34, *p*-value 0.002), as shown in (Table 1). Concerning PTH levels, the disease group 1 shows significantly higher PTH value as compared to the control group (174.7 ± 167.4 vs 27.8 ± 10.9, *p*-value < 0.001), as shown in (Table 1). Concerning MCP-1 levels, the disease group 1 shows significantly higher MCP-1 value as compared to the control group (107.8 ± 155.1 vs 51.8 ± 88.5, *p*-value < 0.001), as shown in (Table 1).

Table 1. Laboratory data expressed as Mean±SD

Parameters	Disease group (n=30)	Control (n=34)	*p*-Value
Urea	117.5 ± 39	20.6 ± 6.7	<0.0001
Creatinine	7.5 ± 2.1	0.8 ± 0.2	<0.0001
eGFR	8 ± 3.3	106.1 ± 22.7	<0.0001
Systolic	144.6 ± 16.5	121.1 ± 3	<0.0001
Diastolic	86.3 ± 13.8	80.7 ± 1.9	0.031
Vit D	30.4 ± 15.94	34.6 ± 17.34	0.001
PTH	174.7 ± 167.4	27.8 ± 10.9	0.001
MCP-1	107.8 ± 155.1	51.8 ± 88.5	< 0.001

No statistically significant correlation was found between MCP-1 levels and renal function markers (urea, creatinine, eGFR), blood pressure (systolic or diastolic), or vitamin D levels (p>0.05 for all). A borderline positive correlation was observed between MCP-1 and parathyroid hormone (PTH) levels (r = 0.167, p= 0.059). as in (Table 2). Suggesting a potential inflammatory interaction with mineral-bone disorder in ESRD, though this did not reach statistical significance.

Table 2. Correlation between serum MCP-1, renal, and hemodynamic parameters in patients

Parameters	MCP-1	
	r	***p*-value**
Urea	0.002	0.980
Creatinine	0.081	0.361
eGFR	-0.055	0.535
Systolic	0.106	0.233
Diastolic	0.002	0.981
Vit D	0.030	0.734
PTH	0.167	0.059

The Receiver Operating Characteristic (ROC) Analysis table for the effect of the factor on predicting the degree of kidney failure (Kidgo Class) progression Systolic value for the patient (cut-off point>121) is considered sensitive and has a specific effect in patients with renal failure (AUC = 0.759, sensitivity = 88.89, specificity = 48.48, p-value = 0.0017) as in (Table 3) . Vit D value for the patient (cut off point >37) is considered sensitive and has a specific effect in patients with renal failure (AUC = 0.732, sensitivity = 88.89, specificity = 63.64, p-value = 0.006) as in (Table 3) . The PTH value for the patient (cut-off point >39) is considered sensitive and has a specific effect in patients with renal failure (AUC = 0.946, sensitivity = 100, specificity = 87.88, p-value = <0.0001) as in (Table 3). MCP-1 value for the patient (cut-off point ≤7.408) is considered sensitive and has a specific effect in patients with renal failure (AUC = 0.700, sensitivity = 77.78, specificity = 72.73, p-value = 0.0220) as in (Table 3).

Table 3. The Receiver operating characteristic (ROC) analysis table

Parameters	AUC	Cut-off point	Sensitivity %	Specificity %	*p*-value
Urea	0.603	>19.8	66.67	69.70	0.4034
Creatinine	0.564	≤0.55	33.33	93.94	0.6178
eGFR	0.608	≤72	33.33	96.97	0.3837
MCP-1	0.700	≤7.408	77.78	72.73	**0.0220**
Systolic	0.759	>121	88.89	48.48	**0.0017**
Diastolic	0.510	>84	22.22	100.00	0.9394
Vit D	0.732	>37	88.89	63.64	**0.006**
PTH	0.946	>39	100.00	87.88	**<0.0001**

Discussion

The primary tasks of the kidneys are excreting waste materials, regulating water homeostasis, and managing blood pressure. End-stage renal disease (ESRD) is a severe condition necessitating prompt intervention, including dialysis or kidney transplantation [13]. A decline in various filtration markers, such as estimated GFR (eGFR), is consistently associated with increased ESRD risk. As in the current study, an increase in renal function tests, elevated serum urea, serum creatinine, and eGFR, as seen in (Table 1), leads to ESRD. That agrees with the Rebholz et al., study [14]. Hypertension is a significant risk factor for end-stage renal disease (ESRD), with various studies highlighting its impact on kidney health. In this current study, elevation in blood pressure contributes to renal deterioration, which agrees with the current findings. That is alien with Kim et al., [15], which found that higher hypertension exposure (systolic BP ≥ 140 mmHg) was linked to increased ESRD risk.

As in (Table 3) the Receiver Operating Characteristic (ROC) analysis supported these findings. Systolic blood pressure demonstrated moderate diagnostic accuracy. A cut-off point of >121 mmHg yielded a high sensitivity (88.89%), although the specificity was modest (48.48%). This pattern favours its use as a screening tool: systolic BP can detect most individuals with CKD or ESRD. The lowest Vitamin D level is in the disease group (ESRD), while the highest is in the health control group as in (Table 1). The normal value for vitamin D in healthy adults is generally considered to be between 75-125 nmol/L (30-50 ng/mL), In patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD), the target levels for vitamin D are higher due to the increased risk of secondary hyperparathyroidism and associated complications [16].

Vitamin D is a lipid-soluble hormone that binds with receptors to help the body maintain calcium and phosphate balance, control bone formation, enhance cardiovascular function, and protect the kidneys. There is growing evidence that vitamin D has a protective effect on the kidneys. Although the exact method is unknown, it might entail lowering oxidative stress levels, increasing the number of podocytes, decreasing podocyte damage, suppressing pro-inflammatory cytokines, and inhibiting the action of the renin-angiotensin system [17]. Patients undergoing hemodialysis frequently show

low vitamin D levels, which correlate with elevated parathyroid hormone (PTH) levels, as shown in (Table 1) [18]. The Cut-off point for Vitamin D is >37 ng/mL, which is more common in healthy individuals. This parameter's sensitivity is 88.89%, which is high, but its specificity, 63.64%, is moderate as in (Table 3). The other hormone, PTH, is very high in disease groups, lower in controls.

In ESRD, the glomerular filtration rate (GFR) is reduced, resulting in phosphate buildup and a drop in calcium levels, which promotes PTH secretion. Elevated parathyroid hormone (PTH) levels are a frequent consequence of secondary hyperparathyroidism (SHPT) [16]. Parathyroid hormone (PTH) plays a crucial role in predicting and diagnosing kidney disease, particularly chronic kidney disease-mineral and bone disorder (CKD-MBD). The Cut-off point is >39 pg/mL, which effectively distinguishes diseased from healthy individuals. At the same time, the sensitivity is 100%, which detects all diseased cases, and the specificity is 87.88%, which has few false positives as in (Table 3). Elevated MCP-1 in the disease group (ESRD), as in (Table 1) suggests A high and variable level of inflammation in ESRD patients. MCP-1 is known to increase in chronic kidney disease due to renal inflammation, immune activation, and oxidative stress. High levels of MCP-1 are linked to increased cardiovascular mortality and atherosclerosis in ESRD patients [19]. Plasma MCP-1 levels are higher with lower eGFR and across higher CKD stages, but do not correlate with albuminuria in CKD patients. The cross-sectional study, Gregg et al., states this It found that plasma MCP-1 was elevated in 81 hemodialysis patients compared to controls [11].

MCP-1 has made significant progress in the field of primary kidney diseases. As a biomarker, it is closely linked to the severity and stage of nephropathy, as well as the disease's occurrence, progression, and prognosis. MCP-1 shows acceptable diagnostic performance (AUC = 0.70), with A cut-off ≤7.408. This is unexpected, since MCP-1 is an inflammatory marker and typically elevates in disease states like ESRD. The sensitivity of this marker is 77.78%. This means the test correctly identifies almost 78% of patients with the condition. The Specificity is 72.73%. This means the test correctly identifies ~73% of those without the condition as in (Table 3).

CONCLUSION

Fundamental Finding : This study demonstrates that patients with end-stage renal disease (ESRD) undergoing hemodialysis have significantly lower serum vitamin D levels and elevated MCP-1 concentrations compared to healthy individuals, suggesting a clear disruption in mineral metabolism and heightened inflammatory activity. These findings are statistically significant and supported by ROC analysis, which confirms the diagnostic utility of these biomarkers, particularly PTH, followed by vitamin D and MCP-1. **Implication :** The results underscore the potential of integrating vitamin D and MCP-1 monitoring into clinical practice as supplementary indicators for assessing nutritional deficiencies and inflammatory burden in ESRD patients, thereby contributing to more personalized and targeted interventions. **Limitation :** However, the study is limited by its relatively small sample size and cross-sectional design, which restrict the ability to draw causal inferences or assess long-term biomarker trends. **Future Research**

: Future investigations should employ larger, multi-center, and longitudinal studies to validate these findings and explore the mechanistic pathways linking vitamin D and MCP-1 with ESRD progression, potentially enhancing early detection and therapeutic strategies.

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* **Haneen Husham Fadhil (Corresponding Author)**
University of Basrah, Iraq
Email: haneenfadhil007@gmail.com

Rana Dawood Salman
University of Basrah, Iraq
Email: rana.salman@uobasrah.edu.iq

Jubran Khaleel Hasan
University of Basrah, Iraq
Email: jubran.hassan@uobasrah.edu.iq