International Journal of Health Systems and Medical Sciences
ISSN: 2833-7433
Volume 03 Number 04 (2024)
Impact Factor: 10.87
SJIF (2023): 3.656

https://journal.academicjournal.id/index.php/ijhsms/index

Article

Prevalence of Hyperparathyroidism among Dialysis Patients in Baghdad Teaching Hospital

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Abstract: Chronic kidney disease is common due to the high prevalence of its main causes. Many pathological changes occur in these patients. Hyperparathyroidism is one of the most common pathologies reported in chronic kidney disease patients. High prevalence rates have been reported worldwide in previous studies, and different factors have been implicated to be associated with Hyperparathyroidism. The aim of this study is to assess the prevalence of hyperparathyroidism among Iraqi patients with chronic kidney disease on hemodialysis therapy and to identify the factors associated with hyperparathyroidism. This was a cross-sectional study with analytic utility performed in in Baghdad Teaching Hospital, Dialysis Center during the period from June 2020 to March 2021. The study included 100 patients (60 males and 40 females). Patients with one or more of the following were excluded: primary hyperparathyroidism. Known parathyroid gland disease, malignancy, bone diseases, Kidney transplantation, or history of parathyroid surgery. Data was collected using a data collection form, and analysis was performed using the statistical package for Social Sciences version 26 (SPSS 26). Appropriate statistical tests were applied accordingly at a level of significance of 0.05. The mean age of the patients was 53.1 ± 14.2 (range: 18 – 80) years, male to female ratio was 1.5 to one. Prevalence of hyperparathyroidism was 33%. No significant association between hyperparathyroidism and each of age, the cause of CKD, or comorbidities. Hyperparathyroidism was more frequent in females (P<0.05). Higher prevalence of Hyperparathyroidism was reported among users of calcium tab supplementation\chelating, vitamin D, and Cinacalcit (P<0.05). Hyperparathyroidism was frequent among Iraqi CKD patients treated by hemodialysis in a rate of 33%. Higher prevalence of Hyperparathyroidism appeared to be associated with female gender, longer duration on hemodialysis, using calcium supplementation/chelating, vitamin D, and Cinacalcit.

Keywords: Chronic kidney disease, Epidemiology, Parathyroid hormone, Hyperparathyroidism, Pathogenesis, Prevalence

Citation: Hussein, A. J., Rasheed, J. I., & Noaman, B. M. Prevalence of Hyperparathyroidism among Dialysis Patients in Baghdad Teaching Hospital. International Journal of Health Systems and Medical Sciences 2024, 3(4), 330-338.

Received: 8th Sept 2024
Revised: 15th Sept 2024
Accepted: 22nd Sept 2024
Published: 29th Sept 2024

1. Introduction

Chronic kidney disease (CKD) is one of the significant health problems worldwide. The prevalence of CKD is increasing due to the high prevalence of its main causes, especially diabetes mellitus, hypertension, and atherosclerosis. In general, it can be assumed that 150 per million people develop chronic kidney disease each year, but it is much more common in old age and occurs in 30% of people over 65. Chronic kidney disease (CKD). Is a large group of diseases that have different causes but are combined by having a long course (more than three months) and a tendency to progress to complete loss of kidney function. Continuous improvement of the nephroprotective strategy and methods of dialysis therapy has significantly improved the prognosis in CKD. However, the progression of complications of CKD - arterial hypertension and associated cardiovascular diseases, anemia, and bone mineral disorders - continues to significantly affect the medical and social rehabilitation and survival of patients. It should be noted that success has already been achieved in the treatment of such serious complications of CKD as anemia and arterial hypertension, and therefore, clinicians have focused on solving another problem - bone mineral disorders in CKD [1–3].

Disorders of calcium metabolism (hypo- or hypercalcemia), hyperphosphatemia, deficiency of active vitamin D, and disorders of parathyroid hormone secretion (secondary or tertiary hyperparathyroidism). Renal osteodystrophy is a progressive disorder of bone structure due to too fast (cause - hyperparathyroidism) [4, 5].

Phosphorus and parathyroid hormone (PTH) level control is important in patients with CKD. Dietary phosphorus restriction, phosphorus-binding agents, vitamin D, calcimimetics, and their combinations are common in these patients [6, 7].

Dialysis treatment is also effective in controlling phosphorus and PTH. However, despite all these treatments, PTH control continues to be an important problem in CKD patients. Parathyroidectomy is used as a last resort in these patients. This process is an attempt that requires experience. In this review, parathyroid gland, secondary hyperparathyroidism, parathyroidectomy indications and techniques in dialysis patients [8, 9].

The past decade has changed significantly the understanding of the pathophysiological processes leading to the development of secondary hyperparathyroidism in patients with chronic renal failure (CRF). Secondary hyperparathyroidism is a frequent and formidable complication of chronic renal failure and develops as a result of relative or absolute deficiency of calcitriol and impaired calcium and phosphorus homeostasis [10, 11].

It is rather difficult to judge the prevalence of secondary hyperparathyroidism in dialysis centers, including domestic ones. First, this is due to the fact that the world's leading experts in this field recommend different target blood levels of PTH, calcium, and phosphorus for patients with CKD. Secondly, in dialysis centers, the dynamic determination of these biochemical markers of mineral and bone disorders (mainly PTH) is difficult [12, 13].

The prevalence of secondary hyperparathyroidism among patients with CKD varies according to the stage of CKD, receiving treatment with programmed hemodialysis - or peritoneal dialysis; however, in several centers, there is a fairly high prevalence of the disease - up to half of all patients need prevention of the development and treatment of hyperparathyroidism. In the last decade, there have been reports of a decrease in the prevalence of secondary hyperparathyroidism. This seems to be quite reasonable and may be related to several points [14–17]. The most serious manifestations of secondary hyperparathyroidism are vascular calcification, a decrease in bone mineral density, and bone damage [18–20]. Diagnosis of secondary hyperparathyroidism is based on the elevated blood levels of PTH. However, the target values of the hormone are set depending on the state of renal function. Serum calcium is either within the target range or tending to decline.

Despite the fact that hyperparathyroidism is common in CKD patients, studies that assess its prevalence among Iraqi patients are scarce, and further studies are still required

and suggested. Therefore, we aimed to assess the prevalence of hyperparathyroidism among Iraqi patients with CKD on hemodialysis therapy and to identify the contributing factors.

2. Patients and Methods

This was a cross-sectional study with analytic utility performed in in Baghdad Teaching Hospital, Dialysis center during the period from June 2020 to March 2021, included a total of 100 Iraqi patients (60 males and 40 females) with CKD and being on hemodialysis

Inclusion Criteria

Adult Iraqi CKD patients treated with conventional intermittent hemodialysis of both genders, regardless of their disease or hemodialysis duration, were included.

Exclusion Criteria

Patient with one or more of the following was excluded: primary hyperparathyroidism, known parathyroid gland disease, malignancy, bone diseases, kidney transplantation, or having a history of parathyroid surgery.

Data Collection

Data is collected through detailed history and through physical examination of patients. The demographic, clinical, and laboratory parameters data were reported.

Routine investigations were performed for all patients, including complete blood count, blood sugar, renal function study, serum sodium, and potassium. Moreover, lipid profile, calcium, and phosphorus were investigated. Additionally, urinalysis, radiographic imaging, ECG, and other investigations were performed accordingly.

Levels of serum Parathyroid hormones was measured using standard methods in the Teaching Laboratory Department.

Standard CKD patient's cutoff values and reference ranges of studied parameters were depended.

Statistical analysis was performed using the statistical package for Social Sciences version 26 (SPSS 26). Cross-tabulation was used to assess the association between Hyperparathyroidism and other variables. Statistical tests were applied according to the type of variables; the Chi-square test was used for categorical (qualitative) variables, and Fisher's exact test was used as an alternative when the chi-square was inapplicable. For scale, (quantitative) variables comparison of means was performed using Student's t test. Level of significance (P-value) was set at ≤ 0.05.

3. Results

The mean age of 53.1 ± 14.2 (range: 18 – 80) years. Majority of the patients were older than 40 years. Males represented 60% of the studied group, with a male-to-female ratio of 1.5 to one. Diabetes mellitus was the commonest cause of CKD among the studied group, contributed for 40%, followed by hypertension in 7%, and other causes were less frequent (Table 1).

Table 1. Age, gender, and causes of CKD of the studied group (N=100)

Variable		No.	%
Age (year)	≤ 40	16	16.0
	41 - 50	27	27.0
	51 - 60	19	19.0
	61 - 70	30	30.0
	> 70	8	8.0
	Mean (SD*)	53.1 (14.2)	-
Gender	Male	60	60.0
	Female	40	40.0
	Ratio: 1.5:1.0	-	-
Cause of CKD	Diabetes Mellitus	40	40.0
	Hypertension	7	7.0
	APKD	5	5.0
	Con dysplasia	4	4.0
	FSGS	3	3.0
	SLE	3	3.0
	Others	10	10.0
	Unknown	28	28.0

PKD: polycystic kidney disease; FSGS: focal segmental glomerulosclerosis;
SLE: Systemic lupus erythematosus

The Prevalence of hyperparathyroidism among the studied group was 33% (Figure 1).

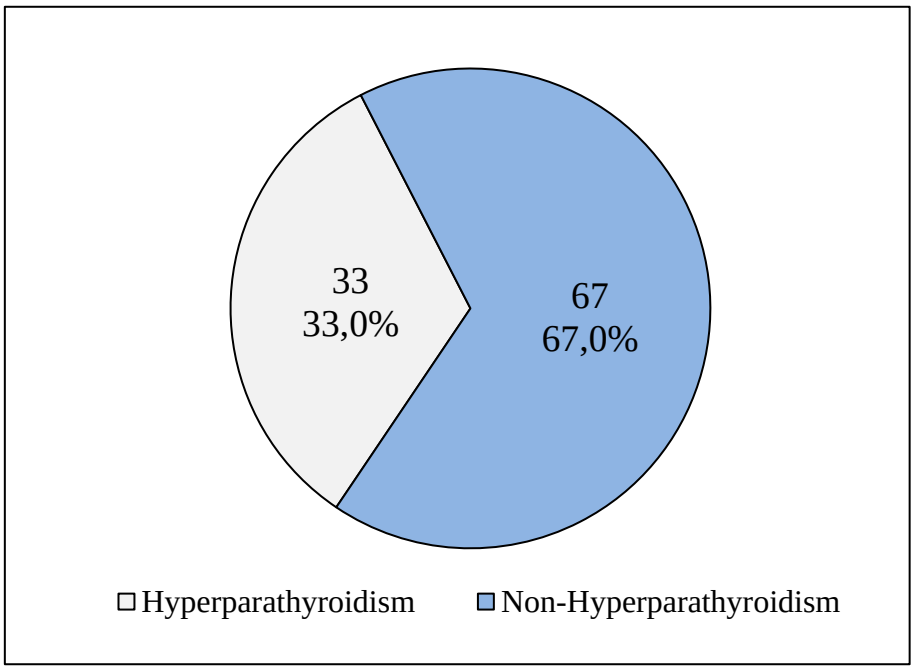

Figure 1. Prevalence of hyperparathyroidism among the studied group

As shown in (Table 2), there is no significant association between hyperparathyroidism and the age of the patients (P>0.05). Hyperparathyroidism was significantly more frequent in females than males, 45% vs. 25%, respectively (P< 0.05). No significant association was found between hyperparathyroidism and each of the causes of CKD and comorbidities (P>0.05). Hyperparathyroidism was significantly more frequent among patients who used oral calcium, vitamin D, and Cinacalcit (P<0.05); no significant association was found with the use of sevelamer (P>0.05). A significant association was found between high ALP level and high rate of Hyperparathyroidism (P<0.05); no significant association was found with the number of HD sessions per week (P>0.05).

Table 2. Cross-tabulation for the association between Hyperparathyroidism and other variables

Variable		Hyperparathyroidism (n=33)		No Hyperparathyroidism (n=67)		Total	P-Value
		No.	%	No.	%		
Age (year)	≤ 40	7	43.8	9	56.3	16	0.667
	41 - 50	9	33.3	18	66.7	27	
	51 - 60	6	31.6	13	68.4	19	
	61 - 70	10	33.3	20	66.7	30	
	> 70	1	12.5	7	87.5	8	
Gender	Male	15	25.0	45	75.0	60	0.037
	Female	18	45.0	22	55.0	40	
Cause of CKD	DM	11	27.5	29	72.5	40	0.637
	Hypertension	2	28.6	5	71.4	7	
	APKD	1	20.0	4	80.0	5	
	Con dysplasia	1	25.0	3	75.0	4	
	Other	5	31.3	11	68.8	16	
	Unknown	13	46.4	15	53.6	28	
Having Comorbidities		30	34.5	57	65.5	87	0.415*
Medication/agent Used by patients	Calcium tab	27	40.3	40	59.7	67	0.043
	Vitamin D	18	51.4	17	48.6	35	0.004
	Sevelamer	12	38.7	19	61.3	31	0.416
	Cinacalcit	6	100.0	0	0.0	6	0.001
HD sessions per week	Two	27	32.9	55	67.1	82	0.974
	Three	6	33.3	12	66.7	18	
ALP level	High	25	47.2	28	52.8	53	0.001
	Normal	8	17.0	39	83.0	47	

*Fisher's exact test was used in comparison, and chi-square was used in other variables

Comparison of duration on HD and laboratory parameters levels between patients with vs. those without hyperparathyroidism revealed that patients with Hyperparathyroidism had significantly longer duration on HD, lower Kt/V ratio, higher creatinine level, and higher Calcium level than those without Hyperparathyroidism, in all comparisons,

(P< 0.05). No significant difference was reported in levels of Albumin, PO4 and Ca x Po4 between the two subgroups, (P>0.05), (Table 3).

Table 3. Comparison of mean levels of laboratory parameters and disease duration across the Hyperparathyroidism status

Variable	Hyperparathyroid-ism (n=33)		No Hyperparathy-roidism (n=67)		P-Value
	Mean	SE	Mean	SE	
Duration on HD (Year)	3.2	0.4	2.9	0.3	0.025
Kt/V	1.10	0.04	1.21	0.03	0.033
Albumin (g/dL)	3.9	0.1	3.8	0.1	0.386
Creatinine	9.1	0.5	8.1	0.3	0.040
PO4 mg/dl)	5.4	0.3	5.1	0.2	0.373
Calcium (mg/dl)	9.0	0.1	7.5	0.2	0.001
Ca x Po4 product(mg^2/dL^2.)	42.57	2.75	40.53	1.80	0.526

4. Discussion

There is a large amount of evidence indicates that patients with end-stage renal diseases on hemodialysis have multiple changes in the functions of many body organs and systems. Parathyroid dysfunction is common among ESRD patients on HD [19].

Previous studies reported higher prevalence rates of hyperparathyroidism among patients on HD [14, 15, 21, 22]; however, despite the higher prevalence of chronic renal failure, particularly in older populations, little data are available on the prevalence of hyperparathyroidism among ESRD patients on HD [23].

According to the definition of hyperparathyroidism, the present study found that 33% of CKD patients on HD had hyperparathyroidism, and the overall mean PTH was 475 pg/ml. There is wide variation in the reported rates of hyperparathyroidism among different studies; in Argentina, Douthat et al. [11] included 1210 patients from 25 centers of dialysis and found that the rate of hyperparathyroidism ranged between 19% to 37.5%%.

Much higher prevalence rate of hyperparathyroidism was reported by Haddad et al. [21], where 77.6% of their patients had hyperparathyroidism. An Earlier study conducted by Owda et al. [10] found that 78% of hemodialysis patients had hyperparathyroidism. Dayma et al. [24] reported a prevalence rate of 72% in north India.

A lower rate of 22% was reported by Shankar et al. in 2019 [25].

The variation in the prevalence rates reported in different studies could be attributed to the variation of case definition used in different studies and the cutoff point of PTH levels used to diagnose hyperparathyroidism in addition to ethnic variations of different populations [10].

Regarding the factors that associated with elevated PTH, we found that the rate of hyperparathyroidism was not significantly associated with the patient's age (P> 0.05), which is supported by the findings of Bureo et al. [22] and Shankar et al. [25].

We found that females had a higher prevalence rate of hyperparathyroidism than males, 45% vs. 25%, respectively (P< 0.05). Nonetheless, there is low evidence about the association between gender and the prevalence of hyperparathyroidism.

On the other hand, Mansour et al. [26] found that hypocalcaemia and CKD stage were significant predictors of hyperparathyroidism, while neither gender, phosphate level, vitamin D level, nor DM being associated with higher rates of hyperparathyroidism.

In contrast, a recent study conducted by Xu et al. [27] found that younger patient's age, male gender, and DM were significantly associated with a higher rate of hyperparathyroidism.

We found no significant association between the prevalence of hyperparathyroidism and each of the causes of CKD and associated comorbidities (P>0.05). Using calcium supplementation, vitamin D and Cinacalcit appeared to be significantly associated with a higher rate of hyperparathyroidism. Previous literature mentioned different therapeutic measures and agents to correct the mineral metabolism disorders in such patients, and there are different pathophysiological mechanisms for the correlation between calcium, vitamin D, phosphate, and PTH [28]; however, calcium supplementation must reduce the PTH level, but this was not the case in our study, this could be explained by the unknown duration of calcium supplementation and when the hyperparathyroidism diagnosed, so the temporal relationship could not be approved, this is one of the limitations of cross-sectional studies. Additional explanation is the fact that the majority of our patients received calcium.

Number of HD sessions per week did not affect the prevalence of hyperparathyroidism. Conversely, the longer duration on HD was significantly increase the prevalence of hyperparathyroidism; patients with the longer duration on HD had a higher rate of hyperparathyroidism.

Zhan et al. [29] documented that longer hours on HD decrease phosphate levels but have minimal change on PTH and calcium levels. Haddad et al. [21] found that a longer duration on HD is associated with a higher rate of hyperparathyroidism. These findings reflect that a longer duration of hemodialysis is associated with more frequent complications despite the different clinical interventions.

5. Conclusion

Hyperparathyroidism was frequent among Iraqi patients with CKD managed by hemodialysis. The reported Hyperparathyroidism rate was 33%, and it was comparable to that in some countries while different than other countries. Higher prevalence of Hyperparathyroidism appeared to be associated with female gender, longer duration on hemodialysis, using calcium supplementation\chelating, vitamin D, and Cinacalcit. Prevalence of Hyperparathyroidism not significantly affected by other variables and parameters. According to the conclusions of our study, we recommend that all available effort and attention must be directed toward reducing the prevalence of hyperparathyroidism among HD patients. Hence, early referral to a nephrologist and adherence to dialysis guidelines are highly suggested. We also suggest a regular and frequent assessment of PTH for early detection and correction of hyperparathyroidism. However, further studies, including other dialysis centers are highly suggested.

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