World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Hemodialysis and thyroid disorders in chronic kidney disease patients at General Hospital of Douala, Cameroon

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World Journal of Advanced Research and Reviews, 2023, 18(02), 1305–1313

Publication history: Received on 17 April 2023; revised on 24 May 2023; accepted on 27 May 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.2.0998

Abstract

Background: kidneys' physiology is related to thyroid hormone functions. They play an important role in certain pathways of these hormones. Therefore the decline in renal function is accompanied by changes in thyroid function. Thyroid abnormalities are described in chronic hemodialysis but insufficiently elucidated in our area. Hence our interest was to evaluate thyroid function in chronic kidney disease patients to point out the implication of hemodialysis on thyroid dysfunction in our population.

Method: we carried out a thyroid function test on a chronic hemodialysed patient admitted at Douala General Hospital (DGH) nephrology service for chronic kidney failure. Samples collected were tested for thyroid hormones total T3 (triiodothyronine), total T4 (thyroxine), and TSH (Thyroid Stimulating Hormone) using enzyme-linked immunosorbent assay (ELISA) technic. Epi Info was used for statistical analysis and 0.05 was significance threshold.

Results: most of the participants were male-gendered (62.2%). The mean age was 49 years (41 ± 12.90) ranging from 20 and 79 years. Thyroid profile analysis of each patient highlighted 30 cases of hypothyroidism (36.59%) and 2 cases of hyperthyroidism (2.44%) out of the 82 enrolled subjects. Besides, our results showed that the duration of dialysis (P = 0.019) and old age (P = 0.04) were risk factors associated with hypothyroidism. Other factors such as gender and clinical history had no impact on the patient's thyroid status.

Conclusion: our study indicated that hypothyroidism is a common endocrine disorder in patients who were going through chronic hemodialysis. A large population size study can be useful to set up systematic thyroid hormone checkups among chronic hemodialysis patients to improve population health conditions.

Keywords: Chronic Kidney Disease (CKD); Hemodialysis; Hypothyroidism; Hyperthyroidism; Thyroid dysfunction

1. Introduction

Chronic kidney disease (CKD) is a permanent structural and/or functional kidney dysfunction. Those abnormalities have to last for at least 3 months (1). Chronic kidney failure is a public health concern around the world. High, middle, and low-income countries are facing the challenges of CKD regularly (2). The prevalence of CKD worldwide is about 7–12% for all stages (1). Biological features of CKD are a decrease in glomerular filtration rate (GFR), proteinuria, decrease in creatinine and urea clearance, among others (3, 4). CKD is associated with many endocrine disruptions such as thyroid gland dysfunction (1, 5). The thyroid is an endocrine gland that secretes the hormones triiodothyronine (T3) and thyroxine (T4). Besides, thyroid function is related to kidney physiology (6). Thus, decline of renal functions is related to changes in thyroid functions (7, 8). Management of CKD is by kidney replacement therapy, especially for end-

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stage kidney disease (ESKD). This procedure includes dialysis (hemodialysis and peritoneal dialysis). ESKD is an increasing health problem with a high economic burden (3, 4). Hemodialysis is the most common kidney replacement therapy used worldwide (9). It uses concentration gradient differences between two compartments, one of been blood. The process is the passage of molecules with different molecular sizes across a semipermeable membrane, from a compartment with a higher solute content (blood) to the lower concentration compartment. This process mimics the glomerular filtration barrier. Blood waste diffuses from the blood to dialysate due to concentration differences. Ideal hemodialysis should remove low and middle molecular weight uremic toxins such as uric acid, urea, creatinine, inulin, and β2-microglobulin but proteins such as serum albumin (Mw: 67 kDa) must be retained (10). In some lower and middle-income countries access to treatments is a major challenge. In Cameroon, the state of knowledge about thyroid disorders in CKD is not well described. That is why we choose to assess thyroid function abnormalities in chronic hemodialysed patients of Douala General Hospital (DGH), to improve CKD patients' care.

2. Material and methods

We carried out a cross-sectional study at the General Hospital of Douala. Our target population was CKD patients admitted to the nephrology department. All participants were chronic hemodialysed patients. The study lasted about 7 months, from January 8th to July 30th, 2019. We included chronic hemodialysed patients regularly monitored at DGH who gave their consent based on inclusion criteria. Excluded patients were those: who had their thyroid or parathyroid removed (1), who were treated by thyroid hormone replacement therapy (2), and finally patients who had prior thyroid dysfunction condition. A survey form was given to the participant and was filled out by each one of them before blood sample collection. Sample-specific volume was collected in a dry tube container. Before blood collection, patients fasted for at least 8 to 12 hours and rested for 15 to 30 minutes. Collected blood was centrifuged for 10 minutes at 3000 rpm and sera were separated from the pellet. Sera were analyzed by ELISA (Enzyme-Linked Immuno Sorbent Assay) technic using Foresigh® Thyroid EIA Test kit for TSH (TSH test by EIA, reference: I231-3011. 96 tests), total T4 kit (TT4 test by EIA, reference: I231-3021. 96 tests) and total T3 kit (TT3 test by EIA, reference: I231-3041. 96 tests). Micro wells were read by spectrophotometer at 450 nm wavelength.

Data collected from filled questionnaires were inputed into Microsoft Office Excel 2013 software and were processed by the same tool. Epi info was used for data analysis. Quantitative data were analyzed and compared using Khi-square and Student T-test. Pearson test was used to compare different groups to highlight a correlation between thyroid parameter values with other variables. A P-value of 0.05 was the threshold of statistical significance.

3. Results

3.1. Sociodemographic population description

Data analysis showed that out of 82 chronic hemodialysed enrolled patients 51 were males (62.2%) and 31 were females (37.80 %). The sex ratio was 1.65 men/women. The studied population was mostly represented by men and the average age was 49 years (41±12.9 years) ranging from 20 to 79 years. Patients aged ranged between 50 and 59 years (26.83%) were the first to display a high rate of CKD. On the contrary, age ranged from 70 to 79 was less represented. Participants of that age range ratio was 3.66% (Figure 1). Our data highlighted a lower count of old-aged chronic hemodialysed patients admitted at the nephrology department of DGH during the period study.

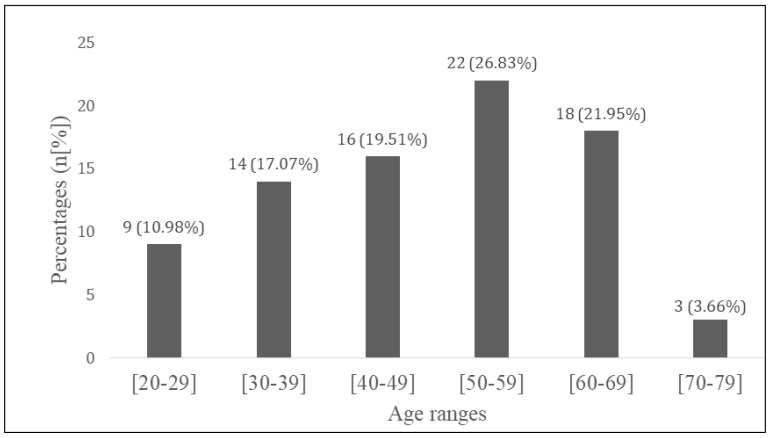


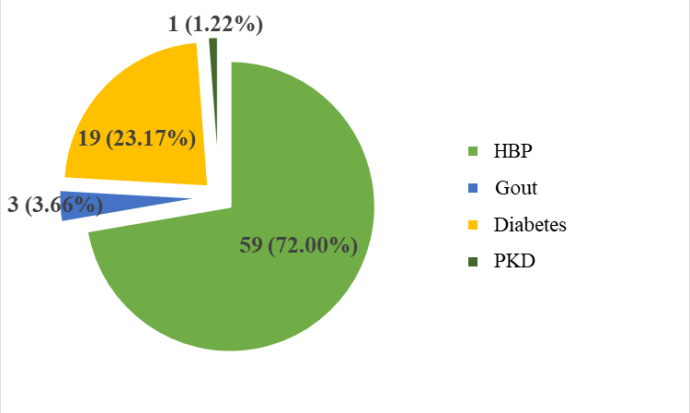
Figure 1 CKD hemodialysed patient ages distribution

CKD Patients were relatively young in the studied population. According to their diet, 63.41% (52/82) of the studied population used to eat freshwater fish while 31.71% (26/82) were using sea salt in their daily diet.

3.2. Clinical conditions description

Aside from suffering from CKD, the studied population displayed other clinical conditions. We assessed the clinical histories of high blood pressure, gout, diabetes, and polycystic kidney disease (PKD). The analysis showed that the majority of our subjects had high blood pressure (72.00%) followed by diabetes (23.17%) (Figure 2). Apart from clinical histories other general clinical signs were evaluated such as palpitations, cramps, edema, and asthenia. The common clinical signs exhibited by most of the participants were asthenia (68.29%) and cramps (54.88%). Palpitation and edema were less observed.

After clinical histories and clinical signs evaluation, we looked at the duration of dialysis. Enrolled chronic kidney disease patients were under hemodialysis for different periods. Some of the patients were following the treatment for less than one year (9.76%). The majority were having hemodialysis for 1 to 4 years (59.76%). The average period of hemodialysis time was 4.21±3.60 years (ranging from 0.5 to 17 years). Only a few patients (2.44%) were treated by hemodialysis for a longer period, 15 to 20 years (Table 1).



HBP: high blood pressure; PKD: polycystic kidney disease

Figure 2 Clinical condition histories

Table 1 Hemodialysis duration distribution

Hemodialysis duration (years)	N	%
[0-1[	8	9.76
[1-5[	49	59.76
[5-10[	19	23.17
[10-15[	4	4.88
[15-20]	2	2.44
Total	**82**	**100.00**

3.3. Thyroid function evaluation: TSH, total T4, and total T3 dosages

TSH and total thyroid hormones T4 (TT4), and T3 (TT3) levels were assessed in each of the participants (Table 2). The analysis showed mean values of TSH: 5.96±98.14 µIU/mL (ranged from 0.01 to 57.60 µIU/mL), total T4: 7.43±2.54 µg/dL (ranged from 2.92 to 14. 88 µg/dL) and total T3: 2.61±5.30 ng/mL (ranged from 0.01 to 34.03 ng/mL). Based on these data, according to thyroid disorders classification criteria, we observed amongst chronic hemodialysed patients 30 cases of hypothyroidism (36.59%), 36 cases of euthyroidism (43.90%) and 2 cases of hyperthyroidism (2.44%). Nevertheless, they were particular patterns of TT3, TT4, and TSH doses whose values did not fit any of the main three classification criteria. Those were counted out. They were 14 out of the 82 enrolled (17.07%) (Table 3).

It was highlighted among participants displaying hypothyroidism an association between hypothyroidism and duration of dialysis (P value=0.019) (Table 4). More the dialysis period was long more the patient's chances to develop hypothyroidism increased. An association of hypothyroidism with factors like sex and age among the studied population was checked. The association between sex and hypothyroidism was not statistically significant (P value=0.38). Nevertheless, an association of hypothyroidism with age was observed (P value=0.04) (Table 5). More the patient is older more cases of hypothyroidism occur among chronic hemodialysed patients.

Aside from dialysis duration, sex, and age, patients' clinical conditions associated with hypothyroidism were closely evaluated. We found no connection between hypothyroidism with these conditions (Table 6).

Table 2 TT3, TT4 and TSH concentration distribution

Hormone concentrations	**N (%)**
TT3 (ng/mL)	
Low (<0.73)	17 (20.73)
Normal (0.73-2.13)	50 (60.97)
High (>2.13)	15 (18.30)
Total	82 (100)
TT4 (µg/dL)	
Low (<4.15)	1 (1.22)
Normal (4.15-14.23)	79 (96.34)
High (>14.23)	2 (2.44)
Total	82 (100)
TSH (µIU/mL)	
Low (<0.25)	5 (6.10)
Normal (0.25-5.0)	43 (52.44)
High (>5.0)	34 (41.46)
Total	82 (100)

Table 3 Thyroid condition classification in CKD

	N	**%**
Euthyroidism	**36**	**43.90**
TSH (normal) TT4 (high) TT3 (low)	4	4.88
TSH (normal) TT4 (normal) TT3 (low)	13	15.85
TSH (normal) TT4 (normal) TT3 (normal)	19	23.17
Hyperthyroidism	**2**	**2.44**
TSH (low) TT4 (high) TT3 (high/normal)	2	2.44
Hypothyroidism	**30**	**36.59**
TSH (high) TT4 (low/normal) TT3 (low)	30	36.59
Particular cases	**14**	**17.07**

Table 4 Hypothyroidism distribution and hemodialysis duration

Hemodialysis duration (years)	Hypothyroidism						P-values
	Yes		No		Total		
	(n)	(%)	(n)	(%)	(n)	(%)	
[0-1[	0	0.00	8	100.00	8	100.00	0.019
[1-5[	16	32.65	33	67.35	49	100.00	
[5-10[	10	52.63	9	47.37	19	100.00	
[10-15[	3	75.00	1	25.00	4	100.00	
[15-20]	1	50.00	1	50.00	2	100.00	

Table 5 Hypothyroidism distribution by sex and ages

	Hypothyroidism						P-value
	Yes		No		Total		
	(N)	(%)	(N)	(%)	(N)	(%)	
Sex							
Female	11	35.48	20	64.52	31	100.00	0.38
Male	19	37.25	32	62.75	51	100.00	
Age							
[20-29]	0	0.00	9	100.00	9	100.00	0.04
[30-39]	3	21.43	11	78.57	14	100.00	
[40-49]	8	50.00	8	50.00	16	100.00	
[50-59]	7	31.82	15	68.18	22	100.00	
[60-69]	10	55.56	8	44.44	18	100.00	
[70-79]	2	66.67	1	33.33	3	100.00	

Table 6 Hypothyroidism distribution with clinical histories

	Hypothyroidism						
Clinical histories	**Yes**		**No**		**Total**		**P-value**
	N	**(%)**	**N**	**(%)**	**N**	**(%)**	
HBP							
Yes	22	36.67	38	63.33	60	100.00	0.43
No	6	27.27	16	72.73	22	100.00	
Diabetes							
Yes	7	36.84	12	63.16	19	100.00	0.48
No	21	33.33	41	66.67	63	100.00	
Gout							

Yes	1	33.33	2	66.67	3	100.00	0.47
No	28	35.44	51	64.66	79	100.00	
PKC							
Yes	0	0.00	1	100.00	1	100.00	0.31
No	0	0.00	0	0.00	0	0.00	

4. Discussion

The socio-demographic data description of the studied population pointed out a sex ratio of 1.65 in favor of men. There were 62.2% of men against 37.8% of females. Many studies highlighted the importance of sex ratio on the men's side. Men are the population displaying the most cases of kidney failure worldwide (9, 11). China Health Insurance Research Association (CHIRA) database showed the dominance of males among kidney disease patients treated by hemodialysis or peritoneal dialysis (11). Nevertheless, another investigation in the same country on hospitalized patients showed that hemodialysis is a more female concern than male's (11). In many other studies on hemodialysis men outnumbered women (9). This observation can be explained by the fact that men's lifestyle is usually less safe (smoking, alcohol, and others) than women's who are less careless about their health. On the other side, the financial burden of hemodialysis is high for individuals with no health insurance, and men are more likely to fund their health care than women whom the most do not have financial freedom, especially in low and middle-income countries.

The most represented population age was relatively young (49 years, 41±12.9 years). Younger ones are the ones targeted by kidney diseases in African countries most of the time. In countries like China patients under hemodialysis where mostly elderly aged above 65 years old, both male and female (11)**.** Likewise, In Europe and America, the majority of chronic kidney disease patients are elderly (65 years +). According to the United Nations Department of Economic and social affairs report, in 2021, life expectancy worldwide was 71.0 years in both sexes. In sub-Saharan African population live less longer (59.7 years) than the European and Northern American population (77.2 years) for example (12). Overall, life expectancy is low in Africa which may explain the younger age of our participants suffering for CKD. Cameroon is a middle-income country where the economic situation is less glorious than in those developed countries. Besides, in developed countries access to healthcare, regular checkup, and follow-ups are facilitated more than in low or middle-income countries where people are not financially stable and some chronic conditions are not early detected or diagnosed. Early detection will prevent kidney disease development, slow disease progression, reduce complications of decreased GFR, reduce the risk of cardiovascular disease, and improve survival and quality of life. In low and middle-income areas, people go to the hospital when their condition is critical, meaning the disease has a great chance to be at an advanced stage at this point.

The clinical background of the participants was checked. High blood pressure, diabetes, and gout were pointed out. Our result showed about 72.00% of chronic kidney disease patients with high blood pressure. In the literature, it was demonstrated that chronic kidney disease is a risk factor for high blood pressure (13). After high blood pressure, diabetes patients were the most represented (23.17%). As HBP, diabetes is also considered a risk factor for developing kidney diseases. A study carried out on type 2 diabetes mellitus patients showed that 41.6% had nephropathy (8). Though, in our study, we did not discriminate diabetes types.

Thyroid dysfunction is considered a chronic kidney disease complication. The case of hypothyroidism is, in most cases diagnosed in chronic kidney disease patients. The level of hypothyroidism increased with the stage of kidney failure. The more the stage is late more the severity of hypothyroidism is noted (7, 8). A Ghananian study on non-dialysis chronic kidney patients at different stages showed only 2% of subclinical hypothyroidism (14). Besides, a study carried out on type 2 diabetes mellitus patients showed that diabetes kidney disease patients displayed 19.7% of subclinical hypothyroidism (8).

In our study, CKD patients treated by hemodialysis thyroid hormones (T3 and T4) and TSH level was evaluated. Results showed a pattern of hypothyroidism, euthyroidism, and hyperthyroidism. The rate of hypothyroidism was 36.59% (30/82). It is not unusual to notice a strong association between hemodialysis and subclinical hypothyroidism in the population with kidney diseases (15). Among those patients, information about their hypothyroidism before reaching the stage of chronic kidney failure and before kidney replacement therapy (hemodialysis) was not mentioned in our investigation. Thyroid dysfunction was reported in many African countries, particularly in the Sub-Saharan region including Cameroon (16). A study carried out in West Cameroon showed a high rate of IDD (Iodine Deficiency Disorders) among which hypothyroidism due to iodine deficiency and thiocyanate overload amongst younger ones (17). The

increased rate of hypothyroidism related to iodine deficiency was described by different authors in the literature (16, 18). In our survey hypothyroidism was related to the duration of dialysis as mentioned by other authors (15). Amiri reported 66.6% of primary hypothyroidism who are having chronic kidney disease and 2.2% of subclinical hypothyroidism (19). Hypothyroidism is common in chronic kidney disease patients with or without dialysis. It is the case of *Srivastava et al.* who found low levels of free T3 in 76.64% of CKD, 70% of low free T4, and high TSH in 26.66% of non-dialyzed patients (20). In our study, we highlighted the fact that more the dialysis period is long more the rate of hypothyroidism is higher. We can not at this stage of our research identify the exact causes of hypothyroidism in CKD. It may be due to hemodialysis nutrient leakage, such as loss of iodine or amino acids during the filtration process. Some dialysis membrane pore size can let pass through molecules like bacterial endotoxin, important plasma protein such as albumin (67 kDa), β2-microglobulin (12 kDa), myoglobin (17 kDa), and interleukin 6 (26 kDa) (21-23). Albumin is a large molecule and should not be filtered. Nevertheless, cases of albumin losses during hemodialysis were reported (23). This observation suggests that during hemodialysis we can notice loss of small or medium size molecules such as hormones. Thyroid hormones T4 and T3 molecular weight are 776.87 Da and 651 Da respectively. They are relatively small molecules. Besides, tyrosine, an amino acid, is an important substrate of thyroid hormone synthesis with a molecular weigh of 181.19 Da. It was proved that high flux membrane hemodialysis is responsible for both total amino acid (TAA) and essential amino acid (EAA) loss (24). Moreover, another thyroid hormone substrate, iodine molecular size is 253.81 Da. Both thyroid hormones and substrates required for their synthesis are relatively small molecules. This suggests that Thyroid hormones or their raw materials, iodine or tyrosine, may pass through the dialysis membrane pores and can lead to hypothyroidism within time. Furthermore, we showed an increasing occurrence rate of hypothyroidism in time depending manner in our study. Another potential cause of hypothyroidism can also be (apart from lack of iodine) selenium deficiency in the population's diet. We noticed in our study that most of the patients included in our study 63.41% (52/82) were used to eat freshwater fish that are not that rich in iodine like sea fish or other seafood and algae. However, 31.71% (26/82) of the participants were using sea salt in their routine diet. Another cause of this hypothyroidism might be an underlying hypothalamus-pituitary-thyroid axis defect or autoimmune condition.

We found 36 cases of euthyroidism (43.90%) and 2 cases of hyperthyroidism (2.44%). As for hypothyroidism, patients with hyperthyroidism may have had the condition before or during the dialysis period. In the literature, some isolated cases of hyperthyroidism were observed in hemodialysed patients (15). *Aryee et al.* in Ghana found the same rate of hyperthyroidism in chronic kidney disease patients (2%) (14). In other cases, 15.5% of primary hyperthyroidism and 6.6 subclinical hyperthyroidism were noted (19).

5. Conclusion

We assessed TSH and thyroid hormone (T3 and T4) levels in chronic kidney disease patients treated by hemodialysis in DGH. Our result showed 36.59% of hypothyroidism. The count of patients with hypothyroidism increased with the duration of hemodialysis and old age. The more the dialysis is long more the patient is at risk of developing hypothyroidism. Hemodialysis could be a risk factor for developing thyroid dysfunction.

Compliance with ethical standards

Acknowledgments

We thank General hospital medical analysis laboratory for the support during experimental phase of our study.

Disclosure of conflict of interest

Authors declared that no conflict interest exist.

Statement of ethical approval

Institutional ethic committee for research on human health of University of Douala had given the authorization N°1784CEI-Udo/04/2019/M to carried out this study. Also the medical director of General Hospital of Douala had approved the study by giving the clearance N°073AR/MINSANTE/HGD/DM/04/19.

Statement of informed consent

Details about the survey were explained to the participants. Each of them agreed by filling and signing the informed consent form.

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