Evaluation of thyroid and parathyroid hormones in children with renal failure treated with hemodialysis

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Abstract:

Kidney disease is a condition in which the kidneys are damaged and can't filter the blood the way they should. This damage can cause wastes and fluid to build up in the body. Kidney disease can also cause other health problems.

Acute kidney injury (AKI) is a sudden decrease in kidney function that usually lasts a short time. Although AKI does not last long, it may cause long-lasting effects even after the underlying problem has been treated. If left untreated, AKI can be life threatening.

Chronic kidney disease (CKD) develops slowly over a long period—usually months to years. CKD may gradually lead to kidney failure. Kidney failure means a person will most likely need a kidney transplant or dialysis soon to stay healthier longer. Kidney failure that is treated with a kidney transplant or dialysis is called end-stage kidney disease, or ESKD.

Kidney disease is not common in children. Researchers don't know exactly how many children are affected by kidney disease because many children have few or no symptoms in the early stages of the disease.

Thyroid hormones affect renal function directly and indirectly. Cardiovascular and renal blood flow mediate indirect effects. Direct impacts are on glomerular filtration rate, tubular secretion and absorption, and hormones. While, Parathyroid hormones regulate calcium and phosphate homeostasis, making it a key regulator of bone and mineral metabolism. PTH is both synthesized and cleaved in the parathyroid gland. PTH is secreted into the extracellular space when storage granules fuse with the outer membrane. Rapidity and regulation by [Ca2+] e in the extracellular environment have been demonstrated for this mechanism in vitro. Most of available information that measured of these hormones and its effects in

adults I the current study the researched will measured activity of these gland in children with renal failure and its effect on others metabolic process in patients.

Method: An observational cohort study was conducted with sample of Iraqi children with renal failure.

Results: significant differences in means were reported in level of thyroid stimulating hormone (-0.69 regarding to TSH), thyroxin (-35.68 for T4),

parathyroid hormone (-210.69 regarding to PTH), and calcium concentration 1.82 in pre and post dialysis.

Conclusion: Thyroid dysfunction is common in patients with chronic kidney disease. There is significant association between thyroid dysfunction and progression of chronic kidney disease, and all patients with end-stage kidney disease were suffering from thyroid abnormality but for lese extend parathyroid dysfunction in patients with renal failure.

Key wards: thyroid gland, parathyroid glands, kidney failure in children, and dialysis.

Introduction:

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for at least three months, with implications for health, CKD have been recognized as significant medical problems for most of the last two centuries (1). Stages of CKD has been advocated by National Kidney Foundation's, Kidney Disease Outcomes Quality Initiative (NKFK/DOQI) to determine the severity of the impaired renal solute clearance (2).

Chronic kidney disease is asymptomatic in its earliest stages (stage I, II). As chronic kidney disease progresses to more advanced stages, signs and symptoms greatly increase it includes: Polydipsia and nocturia, hypertension, anaemia and bone disease, hyperkalaemia, metabolic acidosis, anorexia, nausea and vomiting (3).

From 2020 onward, paediatric kidney disease, particularly End-Stage Kidney Disease (ESKD), continues to be a significant global health concern, particularly in low- and middle-income countries (LMICs). Worldwide, it is estimated that over 15-75 children per million experience chronic kidney disease (CKD), progressing to advanced stages in many cases. A large portion of children diagnosed with CKD already present in stages 3-5 (advanced CKD), where access to kidney replacement therapies (KRT) like dialysis or transplants is crucial.

In LMICs, disparities in access to KRT lead to higher mortality rates. For instance, only about 9-16% of children in African nations receive the required treatments, while in Asia, the range is about 17-34%. High-income countries fare better, with broader access to KRT, but even then, challenges persist in areas with high incidence rates, such as the USA and parts of Southeast Asia (3,4)

In Iraq, chronic kidney disease is increasingly recognized as a public health issue, particularly due to factors like diabetes and hypertension. A 2020 study indicated that the prevalence of CKD in Iraq is rising, and the country faces challenges in providing adequate healthcare resources for managing kidney diseases. International Society of Nephrology highlighted that pediatric kidney care in low- and middle-income countries, including Iraq, faces significant challenges, with limited access to treatments like dialysis and transplantation (5)

Thyroid hormones (TH) are crucial for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of TH, two thirds of catabolism of hormones occurs in the kidneys (6). In patients with CKD, renal clearance decreases at the same time as renal blood flow; as this progresses, renal tubular and peritubular transport of hormones decreases, causing disparity in hormone concentrations (7). Thyroid function tests (TFTs) is a collective term for blood tests used to check the function of the thyroid. A TFT panel typically includes thyroid hormones such as thyroid stimulating hormone (TSH) and thyroxin (T4), and triiodothyronine (T3), they act to increase the basal metabolic rate, affect protein synthesis, help regulate long bone growth (synergy with growth hormone) and neural maturation, and increase the body's sensitivity to catecholamine (adrenaline) by permissiveness(8).

Few studies involving children with CKD found that an incidence of thyroid dysfunction was ranges between 10 and 55%. Additionally, children with CKD in dialysis, the incidence of thyroid dysfunction is high, therefore it is necessary to introduce the assessment of thyroid function in order to improve the overall quality of care of these patients(9,10)

Method:

Thirty children diagnosed as patients' renal failure and need for renal dialysis. The blood sample was taken from the patients to performed ordinary laboratory tests that required from patients before and after dialysis procedure.

After taking verbal consent from the patient by researchers to performed some of laboratory tests, five milliliters of venous blood were collected and placed in a gel tube at room temperature for 15 minutes for clot formation (according to kit sheet). Remove the clot by centrifuging at 3000 rpm for 20 minutes. The serum was divided into four parts and stored in Eppendorf at -20 ºC until used for

estimation of the bone biomarkers required in the study. After this, the blood sample was resorted to a 37 ºC in water bath.

Biomarkers measurement:

All biomarkers were measured by ELASSA method and according to kit sheet.

Study design and setting:

An observational cohort study was conducted with sample of Iraqi children with renal failure.

The sample of the research was collected from different Iraqi cities include holy Karbala, Hilla, and Baghdad.

Inclusion criteria:

the patients included in the study Children were all the children aged les than 18 years old with renal failure and on dialysis.

Exclusion criteria:

1- Patients aged above 18 years.
2- Children with other clinical condition
3- Children having infectious disease
4- Children with renal failure were diagnosed with end stage renal failure and others patients not required dialysis.

Statistical analysis:

The Statistical Package for the Social Science (SPSS, version 22, IBM, New York USA) was used to conduct statistical analyses. Descriptive statistics (means, standers deviations, frequencies and percentage) were measured. Independent T-test were used to measure the difference in means of biomarkers across the participating groups. Paired sample T-test was used to measure the difference in means of biomarkers at baseline and after treatment with dialysis. Finally, the Pearson correlation was used to measure the relationships between the patient parathyroid hormone and calcium level.

Results:

Table 1: characteristic of participant patients:

Number of patients	30	
gender	Femail =9	30%
	Male =21	70%
Age	Minimum	Maximum
	6 years	16 years
Family history	Yes =6	20%
	No=24	80%

Table 2: domenstared mean, number, and stander deviation of the measured biomarkers:

	TSH	T3	T4	PTH	CA	TSH-p	T3-p	T4-p	PTH-p	CA-p
Mean	2.06	1.06	77.45	174.92	9.78	2.75	3.02	113.13	385.07	7.96
N	30	30	30	30	30	30	30	30	30	30
Std. Deviation	1.14	.28	9.52	37.77	1.58	1.10	12.47	22.96	130.76	1.40

TSH: thyroid stimulating hormone, T3: triiodothyronine, T4: thyroxin, and PTH: parathyroid hormone, and CA1: calcium concentration.

Table 2: demonstrated the differences among the measured biomarkers in pre and post dialysis.

		Mean	Std. deviation	p-value
Pair 1	TSH – TSH-2	-.69	1.48	.01
Pair 2	T3 - T3-2	-1.96	12.47	.39
Pair 3	T4 - T4-2	-35.68	22.68	.00
Pair 4	PTH1-PTH-2	-210.67	131.80	.00
Pair 5	CA1 – CA-2	1.82	1.43	.00

TSH: thyroid stimulating hormone, T3: triiodothyronine, T4: thyroxin, and PTH: parathyroid hormone, and CA1:calicium concentration (pre- dialysis)

TSH-2: thyroid stimulating hormone, T3-2: triiodothyronine, T4-2: thyroxin, and PTH-2: parathyroid hormone, CA2: calicium concentration (post- dialysis)

Paired T-test p-value =<0.05

Table 3: demonstrated the relationship between parathyroid hormone and calcium level in pre and post therapy with dialysis.

		PTH-1	CA-1	PTH-P	CA-P
PTH	Pearson Correlation	1	-.095	1	.218
	p-value		.618		.246
	N	30	30	30	30
CA	Pearson Correlation	-.095	1	.218	1
	p- value	.618		.246	
	N	30	30	30	30

PTH-1: Parathyroid hormones, CA-1: calcium concentration in pre-dialysis stat. PTH-P: Parathyroid hormones, CA-P: calcium concentration in post-dialysis stat. Correlation test. p-value=≤0.05

Discussion:

The results that shown in (table 1) demonstrated average mean of the measured biomarkers included in the research. According to the previous studies wide range in the normal average values of the measured biomarkers (11). In Iraq there is no reference values for the levels of thyroid hormones among Iraqi children, in contrast to Pakistan some of studies demonstrated levels of the measured biomarkers according to age group population (12). But because the average of age group of patients included in the study from 9- 14 years old in pre- dialysis and post -dialysis in about upper limit of the normal range according to FSH. while for FT3 slightly elevated in patients after dialysis, this can be attributed to the nature of this type of hormone as highly protein binding and the patients are newly undergoing from aggressive procedure dealing with protein of the blood, for the same reason can be explained why the high level of FT4 as the body not need for conversion of FT4 to FT3.

The concentration of PTH that allows optimum growth is a very important clinical issue, in assessment the function level of parathyroid gland between patients with renal failure the researchers found in pre-dialysis within normal range (in assessment the parathyroid hormone highly differences with age and gender) (13). After dialysis, highly elevated from the value of pre-dialysis this is consistent with the results in the study conducted in 2005(14). From the obtained result can proposed that when PTH concentrations were outside the normal range, which becomes increasingly common as CRF progresses.

In (table 2), according to the paired T-test the result shown significant differences in level of all the measured biomarkers except T3-T3-2 (represented levels of T3in pre-dialysis and T3 in post -dialysis was insignificant changes this may be related to the stage of renal failure, the glomerular filtration rate or for the frequency of dialysis procedure per time unit), in some degree the results was consistent with other study done in 2023 showing the patients with renal failure also have at the same time significant lowering in the thyroid function (16).

According to the statical correlation(table3) between the level of parathyroid and calcium in serum of the patients with renal failure and on dialysis demonstrated no significant relationship between serum calcium concentration and hormone of parathyroid gland, from the obtained fact the changes in the calcium concentration mainly related to effect of the disease and treatment on the patients rather than parathyroid hormone effects.

Conclusion:

From the obtained results all patients with chronic kidney disease and treated by dialysis required to thyroid and parathyroid assessment as the most of patients included in the study demonstrated decrement in thyroid function.

Recommendation:

1-determination the reference values for thyroid and parathyroid hormones in children in relation with age and sex.

2- sample size most be increase time of following of the patients to be more represented.

3- measuring this biomarkers in separated group as in female and male to be more representative.

Ethical approval:

Ethical approval was obtained from Ethical and scientific Committee at the research Ethical Board of Al-Zahrawi University College (REBZ)

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