Thyroid Dysfunction in Children with Chronic Kidney Disease

Saja Asaad Obeed* FIBMS, **Taghreed Fadhill Mohammed*** FIBMS (Neph.), **Juhayna Kifah Abdul-Wahhab** FIBMS(FM)

ABSTRACT

Background: Kidney is involved in the metabolism and elimination of thyroid hormone, two thirds of catabolism of hormones occurs in the kidneys. In patients with chronic kidney disease, renal clearance decreases at the same time as renal blood flow; as this progresses, renal tubular and peritubular transport of hormones decreases, and causing disparity in hormone concentrations.

Objectives: To study thyroid dysfunction in patients with chronic kidney disease.

Methods: A case control study was conducted in the Central Teaching Hospital of Pediatric from first of July 2018 until end of June 2019. Sixty-seven patients aged between 1-14 years who were collected from casualty or emergency units and divided into two groups: Case group 33 patients with chronic kidney disease. Control 34 children. Patients who underwent dialysis, family history of thyroid disorder were excluded from this study. Both groups underwent clinical examination, laboratory investigation (complete blood count, thyroid and renal function tests, general urine examination, and total serum protein) and sonographic examination of kidney.

Results: Means of serum triiodothyronine and thyroxin levels in case group were significantly lower (1.27 nmol/l versus 2.34 nmol/l regarding T3), (86.25 nmol/l versus 111.4 nmol/l regarding T4), while mean of serum thyroid stimulating hormone was significantly higher than that in control group. All patients with stage five suffering from thyroid dysfunction, with a statistically significant association (P= 0.006) between thyroid function and chronic kidney disease stages.

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.

Keywords: Thyroid dysfunction, Chronic kidney disease, Hormones, Iraq.

Iraqi Medical Journal Vol. 69, No. 1, Jan-June 2023; p. 29-36.

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 (NKF-K/DOQI) to determine the severity of the impaired renal solute clearance[2].

Primary causes of CKD in children significantly differ from those for the adult onset of the disease. The main etiologic factors of CKD in children are[3-5]:

- Obstructive nephropathy or reflux nephropathy (75%).
- Congenital anomalies of the kidney and urinary tract (20%-30% of all anomalies).
- Steroid-resistant nephrotic syndrome (SRNS) (10.4%).
- Chronic glomerulonephritis particularly in older children (e.g. lupus nephritis, Alport syndrome) (8.1%).
- Renal ciliopathies (5.3%).

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, anemia and bone disease, hyperkalemia, metabolic acidosis, anorexia, nausea and vomiting[6].

*Dept. of Pediatrics, Central Child Teaching Hospital, Baghdad, Iraq.
Corresponding: Dr. Saja Asaad. Email: sajaasaad89@gmail.com

Table 1: Stages of chronic kidney disease.

Stage	Description	GFR* (ml/min/1.73 m^2)
1	Kidney damage with normal or increased GFR	> 90
2	Kidney damage with mild decrease in GFR	60–89
3	Moderate decrease in GFR	30–59
4	Severe decrease in GFR	15–29
5	Kidney failure	< 15 or dialysis

*GFR = Glomerular filtration rate.

History is of importance in reaching the diagnosis in patients with CKD, which include; family history (consanguinity), antenatal (oligohydramnios), post-natal (respiratory distress), infancy/childhood (polyuria/polydipsia). On examination; especially at birth, looking for; single umbilical artery, palpable bladder, spinal defects, ambiguous genitalia and dysmorphic features. Additionally, short stature, malnutrition and obesity, pallor, edema, flapping tremors, hypertension should be observed[7].

Anemia is an important clinical finding in CKD, and a complete blood cell count is necessary in both in the initial evaluation and follow-up in these children. Serum chemistry provides a valuable diagnostic tool also. Blood urea nitrogen and serum creatinine assessments are the most important tests. Serum sodium, potassium, calcium, phosphorus, alkaline phosphatase, parathyroid hormone and lipid profile are important in the treatment and prevention of CKD and its complications[8].

Management of children with CKD aims at possible interventions to retard progression of disease and the treatment of co-morbid conditions in the early stages. It includes treatment of hypertension, hyperlipidemia, cardiovascular manifestation, anemia, growth disruption, metabolic acidosis and diet regulation[9,10].

All patients with estimated glomerular filtration rate (eGFR) below 20 ml/min/1.73 m^2 and/or who are likely to progress to end-stage renal disease (ESRD) within 12 months should receive education and counseling to aid their selection of the most appropriate renal replacement therapy modality. Additionally, early kidney transplantation may be associated with improved long-term outcome[11,12].

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[13]. 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[14]. 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[15].

The most common kidney derangements associated with hypothyroidism are: elevation of serum creatinine levels, reduction in glomerular filtration rate (GFR) and renal plasma flow, disruption of the capacity to excrete free water and hyponatremia[16]. It is estimated that the prevalence of hypothyroidism among children of school age and adolescents ranges from 1 in 500 (0.2%) to 1 in 1000 (0.1%)[17]. 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[18].

Methods

This is a case control study that was conducted at the Nephrology Department at Child Central Teaching Hospital during the period of year from 1st of July 2018 till end of June 2019. The study included 67 patients aged between 1-14 years who were collected from inpatient ward, casualty units and divided into two groups: Case group included 33 patients who were diagnosed CKD and control group included 34 children who attended the casualty unit for causes other than CKD. Glomerular filtration rate for each child was calculated by the following equation: (The "updated" 2009 Schwartz equation): GFR (ml/ min/1.73 m2) = 0.413 x Height (cm) / Serum Creatinine (mg/dl).

Inclusion criteria for case group

- Known CKD cases.
- On conservative treatment.

Exclusion criteria for both groups

- Patients who underwent peritoneal or hemodialysis.
- Family history of thyroid disorders.
- History of any medication (e.g. steroid) or disease affect thyroid function test (two cases with cystinosis and three with nephrotic syndrome were excluded).
- History of any surgery or radiological intervention to thyroid gland).

All patients' parents were told about the nature of the study and verbal consent was taken from them. History including causes of CKD, duration of illness, history of hypertension, diabetes mellitus or other chronic illness, drug history, nutrition status was taken. Then both groups underwent clinical examination, laboratory investigation and sonographic examination. From all patients, we took blood sample which was sent to laboratory for T3, T4, and TSH. TFT was done by using cobas e 411 fully automated analyzer, which act by electro-chemiluminescence technology "ECL".

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables accordingly. Chi square test was used to assess the association between thyroid function and certain clinical information. Pearson's correlation test (r) was used to assess correlation between continuous variables accordingly. A level of p value less than 0.05 was considered significant.

Results

The age of patients was ranging from 1.2 to 14 years with a mean of 7.18 (± 3.88) years. In both groups, more than half of children were aged between 5-10 years (54.5% in case group and 52.9% in control group), (Table 2).

Males were 72.7% of children with CKD, while 52.9% of those in control group were females, (Table 3).

As shown in table 4, of the 33 patients with CKD, the highest proportion of them (39.4%) were with stage 4, while (33.3%), (15.2%), and (12.1%) were with stages 3, 5, and 2, respectively.

Regarding serum T3, (63.6%) of CKD cases were with low T3 level. All of children in the control group were with normal level of T3. Concerning T4, (75.7%) and (94.1%) of the children in case and control groups, respectively, were with normal level of this hormone. Normal level of TSH was reported among (72.7%) of children with CKD and (76.5%) of the control. It was clear that the mean of serum T3 level in case group was significantly decreased (P= 0.001) than that in control group. Also, there was a statistically significant difference (P= 0.001) in mean of serum T4 levels between the study groups. The mean TSH in case group was significantly increased compared to that in control (3.79 mIu/l versus 2.58 mIu/l) with P value of (0.028), (Table 5).

The distribution of thyroid function in children with CKD was as follows: 6 (18.2%) euthyroid, 16 (48.4%) low T3 syndrome, 3 (9.1%) low T4 syndrome, (Table 6).

As shown in tables 7 and 8, 25% of children with stage 2, revealed low T3 syndrome; 72.7% of children with stage 3 had low T3 syndrome, stage 4; 30.7% low T3 syndrome, 15.4% low T4 syndrome. Concerning stage 5; low T3 syndrome 60%, low T4 syndrome 20%. All patients (100%) with stage 5 were suffering from thyroid dysfunction, with a statistically significant association (P= 0.006) between thyroid function and CKD stages.

It was clear that there was no statistically significant association (P= 0.712) between thyroid function of children with CKD and etiology of this disease.

Table 2: Distribution of study group by age.

Age of children (year)	CKD group	Control group
< 5	18.2 %	29.5 %
5 -10	54.5 %	52.9 %
> 5	27.3%	17.6 %

Table 3: Distribution of study group by gender.

Gender of children	**CKD group**	**Control group**
Male	72.7 %	47.1 %
Female	27.3%	52.9 %

Table 4: Distribution of study patients by stages of CKD.

CKD Stages			
Stage 2	**Stage 3**	**Stage 4**	**Stage 5**
12.1 %	33.3 %	39.4 %	15.2 %

Table 5: Distribution of study groups by thyroid profile.

Variable	**Study groups**		**Total (%) N= 67**	
	CKD Group (%) n= 33	**Control Group (%) n= 34**		**P-Value**
T3				
Normal	12 (36.4)	34 (100.0)	46 (68.6)	
Low	21 (63.6)	0 (0)	21(31.3)	
Mean ±SD	1.27 ± 0.68	2.34 ± 0.97		**0.001**
T4				
Normal	25 (75.7)	32 (94.1)	57 (85.1)	
Low	8 (24.3)	2 (5.9)	10 (14.9)	
Mean ±SD	86.25 ± 26.72	111.4 ± 27.61		**0.001**
TSH				
Normal	24 (72.7)	26 (76.5)	50 (74.6)	
High	4 (12.1)	6 (17.6)	10 (14.9)	
Low	5 (15.2)	2 (5.9)	7 (10.5)	
Mean ±SD	3.79 ± 2.41	2.58 ±1.99		**0.028**

Table 6: Distribution of CKD children by thyroid function.

Thyroid function of Patient					
Euthyroid	**Low T3 syndrome**	**Low T4 syndrome**	**Low T3-low T4 syndrome**	**Subclinical hypothyroidism**	**Subclinical hyperthyroidism**
18.2 %	48. %	9.1 %	15.2 %	6.1 %	3 %

Table 7: Distribution of thyroid function in the case group according to the stages.

Thyroid Dysfunction	CKD Stages				Total (%) n= 33
	Stage 2 (%) n= 4	Stage 3 (%) n= 11	Stage 4 (%) n= 13	Stage 5 (%) n= 5	
Euthyroid	3 (75.0)	1 (9.1)	2 (15.4)	0 (0)	6 (18.2)
Low T3	1 (25.0)	8 (72.7)	4 (30.7)	3 (60.0)	16 (48.5)
Low T4	0 (0)	0 (0)	2 (15.4)	1 (20.0)	3 (9.1)
LowT3_LowT4	0 (0)	1 (9.1)	3 (23.1)	1 (20.0)	5 (15.2)
Subclinical Hypothyroidism	0 (0)	0 (0)	2 (15.4)	0 (0)	2 (6.0)
Subclinical Hyperthyroidism	0 (0)	1 (9.1)	0 (0)	0 (0)	1 (3.0)

Table 8: Association between thyroid function and CKD stages.

CKD stages	Thyroid Function		Total (%) n= 33	P- Value
	Abnormal (%) n= 27	Normal (%) n= 6		
Stage 2	1 (25.0)	3 (75.0)	4 (12.1)	**0.006**
Stage 3	10 (90.1)	1 (9.1)	11 (33.3)	
Stage 4	11 (84.6)	2 (15.4)	13 (39.3)	
Stage 5	5 (100.0)	0 (0)	5 (15.2)	

Table 9: Association between thyroid function and CKD causes.

Variable	Thyroid Function		Total (%) n= 33	P- Value
	Abnormal (%) n= 27	Normal (%) n= 6		
Congenital	14 (82.4)	3 (17.6)	17 (51.5)	**0.712**
Recurrent UTI	2 (50.0)	2 (50.0)	4 (12.1)	
Obstructive Uropathy	5 (100.0)	0 (0)	5 (15.2)	
GN	3 (100.0)	0 (0)	3 (9.1)	
Others Causes	3 (75.0)	1 (25.0)	4 (12.1)	

——————————Discussion

In the present study, mean and standard deviation of age was 3.88± 7.18 years (ranging from 1.2 to 14 years), more than half of children were aged between 5-10 years. Females were 27.3 % of children with CKD while 72.7 % were males, the highest proportion of them 39.4% were with stage 4, while 33.3 %, 15.2%, and 12.1% were with stages 3, 5, and 2, respectively. Different results observed in Tan et al, in which male to female ratio 1.3:1, as male constitute 57.3% from the study patients, in concern to age, mean and standard deviation of age was 11.3 ± 4.12 years (ranging from 1 to 18 years), less than half of children were aged between 5-10 years (33.7%) [20].

Another different results in Gheissari et al, in which mean of age was 12.2 ± 2.4 years (range from 7-18 years), nearly equal male and female prevalence as male

constituted 52.9% of the study patients, with male to female ratio was 1:1.2[21].

In present study, (63.6 %) of CKD children were with low T3 level. All of children in the control group were with normal level of T3. Slightly different results observed by Singh and colleagues[22], in which twenty patients presented with CKD included, they noticed that Serum T3 concentration was less than the T3 normal range in 12 of the 20 patients with CKD (60%). Concerning serum T4, (75.7%) and (94.1%) of patients in case and control group, respectively were with normal level of this hormone; while in Singh and colleagues serum T4 was diminished in 15 (75%) of patients with CKD. Regarding TSH, normal level observed in (72.7%) of children with CKD and (76.5%) of those in control, while (12.1%) of CKD children were with high level of this hormone and (15.2%) of them were with low TSH level, by Singh and colleagues[22] mean serum TSH were within the normal range in CKD group and did not differ from that found in the controls[22].

In this study, mean serum T3 in case group was significantly decreased than that in control (P= 0.001). Also, mean serum T4 decreased significantly in case group as compared to control, this difference was statistically significant (P=0.001). The mean serum TSH was significantly increased compared to that in control group (P = 0.028). These results are in accordance to study by El-Hanna and colleagues, in which the mean serum TSH in children with CKD was 4.36 ± 1.61µIU/l, while in control it was 2.58 ± 0.57 µIU/l, a difference that was statistically significant (P< 0.001), also noticed that mean of serum T3 in CKD cases 113.18 ± 17.13 ng/dl, while in the control children, 131.56 ± 4.26 ng/dl, a difference also statistically significant (p<0.001). The only difference observed in these results was a non-significant decrease in the mean serum T4 levels , as it was 6.15 ± 1.52 ng/dl in case group, while in control 6.33 ± 1.21 ng/dl (p>0.2)[23]. Another agreement observed by Rajeev and colleagues, in which serum T3 was decreased in 88% of CKD patients, as the mean serum T3 was significantly lower than that in the control (P<0.05). Furthermore, (33%) of patients had lower serum T4 than the controls, when mean serum T4 in the CKD patients was significantly lower than that in the control (P <0.002). Finally, the serum TSH was increased in (60%) among those with CKD, as mean serum TSH was significantly increased than that in the controls (P < 0.000) [24].

In this study,(18.2%) of patients were euthyroid; (48.4%) low T3 syndrome, (9.1%) low T4 syndrome, (15.2%) lowT3-lowT4 syndrome, (6.1%) subclinical hypothyroidism, and (3%) subclinical hyperthyroidism. Different results observed in study by Garrido-Magaña and colleagues, in which the majority of patients were diagnosed with subclinical hypothyroidism (64.2%), (21.4%) of them had euthyroid sick syndrome and (14.2%) with primary hypothyroidism. They concluded that dysfunctions affect children in their study contrast with previous studies, in which the most common condition is euthyroid sick syndrome, followed by subclinical hypothyroidism and primary hypothyroidism. This could suggest that CKD in children is associated with a greater incidence of real thyroid dysfunction, rather than a condition that is considered a reaction to a chronic disease, like euthyroid sick syndrome[19].

In this study, stage three (9.1%) euthyroid state, (72.7%) had low T3 syndrome (9.1%) had lowT3-low T4, and (9.1%) had subclinical hyperthyroidism. While stage five, (60%) low T3 syndrome, (20%) low T4 syndrome, and (20%) lowT3-lowT4 syndrome. Different results observed in Fan et al study[25], as found a high prevalence of low T3 syndrome in CKD patients without dialysis, even in early stages (I and II), in which low T3 syndrome observed in (22.2%), (22.5%), (59.6%), (71%) and (76.1%) of patients presented with stage I, II, III, IV and V, respectively, and concluded that increasing prevalence of low T3 as CKD progresses indicates its value as a predictor of worsening CKD [25].

In concern to the association of thyroid function with stage, all patients with stage five were suffering from thyroid dysfunction, with a statistically significant association (P= 0.006) between thyroid function and CKD stages. Similarity to the current results observed in Khatiwada et al[26], in which found that blood urea, creatinine and TSH level increased significantly across CKD stages III–V, concluded that thyroid dysfunction is common in CKD patients and progression of CKD is accompanied by rise in hypothyroidism status [26] . Also, Song and colleagues found that there was an increasing trend for the population of low T3 according to the increase of a CKD stage [27]. The association between causes of CKD and thyroid function showed no statistically significant association (P= 0.712).

In conclusion, Thyroid dysfunction is common in patients with chronic kidney disease, and those patients in state of biochemical hypothyroidism or sick euthyroid. The most prevalent phenotype of thyroid dysfunction in CKD is low T3 syndrome. There is significant association between thyroid dysfunction and progression of CKD, all patients with stage five suffering from thyroid abnormality

Acknowledgment: I would like to thanks Allah for granting me the will to accomplish this thesis and to express my deepest and sincere thanks and gratitude to my supervisor Dr. Taghreed Fadhill Mohammed and Dr. Munaf Faiq for their guidance valuable instruction and constant encouragement during this study.

References

1. Tomlinson LA, Wheeler DC. Clinical evaluation and management of chronic kidney disease. In: Johnson RJ, Feehally J, Floege J (eds.). Comprehensive Clinical Nephrology. 5th ed. Philadelphia: Saunders, Elsevier; 2015. P. 942-947.
2. Chen MLW, Hsu C-Y. Should the K/DOQI definition of chronic kidney disease be changed? Am J Kidney Dis 2003; 42: 623-5.
3. Harambat J, Van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. Pediatric Nephrology 2012;27(3):363-73.
4. Smith JM, Stablein DM, Munoz R, Hebert D, McDonald RA. Contributions of the transplant registry: The 2006 annual report of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS). Pediatric Transplantation 2007;11(4):366-73.
5. Vivante A, Hildebrandt F. Exploring the genetic basis of early-onset chronic kidney disease. Nature Reviews Nephrology 2016;12(3):133.
6. NAPRTCS: 2008 Annual Report. Rockville, MD: EMMES, 2008.
7. Iyengar AA. Foster BJ. Chronic Kidney Disease (CKD). In: Phadke K,Goodyer P.(Ed). Manual of Pediatric Nephrology. Springer-Verlag Berlin Heidelberg 2014. P. 373 -8.
8. Knoyan G. The importance of early treatment of the anemia of chronic kidney disease. Nephrol Dial Transplant 2001; 16 Suppl 5:45-9.
9. United States Department of Agriculture (USDA). National Nutrient Database for Standard Reference, Release 16–1. (accessed October 13, 2005). www.nal.usda.gov/fnic/foodcomp/Data/SR16-1/wtrank/16-1w203
10. Noordzij M, Korevaar JC, Boeschoten EW, Dekker FW, Bos WJ, Krediet RT. The Kidney Disease Outcomes Quality Initiative (K/DOQI) Guideline for Bone Metabolism and Disease in CKD: association with mortality in dialysis patients. Am J Kidney Dis 2005; 46(5):925-32.
11. Gulati S, Langman CB. Chronic Kidney Disease in Children Treatment & Management. Management of Cardiovascular Manifestations, Updated: Feb 21, 2018. https://emedicine.medscape.com/article/984358-treatment#d11
12. Saland JM, Ginsberg H, Fisher EA. Dyslipidemia in pediatric renal disease: epidemiology, pathophysiology, and management. Curr Opin Pediatr 2002; 14(2):197-204.
13. Tamura MK, Vittinghoff E, Yang J, Go AS, Seliger SL, Kusek JW, et al. Anemia and risk for cognitive decline in chronic kidney disease. BMC Nephrology 2016;17(1):13.
14. Iglesias P, Diez JJ. Thyroid dysfunction and kidney disease. European Journal Endocrinology 2009;160(4):503-15.
15. Dayan CM. Interpretation of thyroid function tests. The Lancet 2001;357(9256):619-24.
16. Bowen R. Mechanism of action and physiologic effects of thyroid hormones. Endocrine index. Colorado State University 2010; 24:
17. Montenegro J, Gonzalez O, Saracho R, Aguirre R, Gonzalez O, Martinez I. Changes in renal function in primary hypothyroidism. American Journal of Kidney Diseases 1996; 27: 195-8.
18. Donohoue P. Thyroid gland. In: McMillan JA, DeAngelis CD, Feigin RD, Warshaw JB, (eds.). Pediatrics. Philadelphia: Laippincot Williams & Wilkins; 1999. P. 1808.
19. Garrido-Magaña E, Heyser-Ortiz SE, Aguilar-Kitsu A, Mendoza-Guevara L, Nishimura-Meguro E, Ramírez-Rivera A et al. Thyroid dysfunction in children with chronic renal failure. Nefrología 2009;29(5):449-55.
20. Tan SY, Naing L, Han A, Khalil MAM, Chong VH, Tan JJ Wjon. Chronic kidney disease in children

and adolescents in Brunei Darussalam. World J Nephrology 2016;5(2):213.
21. Gheissari A, Kelishadi R, Roomizadeh P, Abedini A, Haghjooy-Javanmard S, Abtahi S-H, et al. Chronic kidney disease stages 3-5 in Iranian children: Need for a school-based screening strategy: The CASPIAN-III Study. Int J Prev Med 2013;4(1):95-101.
22. Singh PA, Bobby Z, Selvaraj N, Vinayagamoorthi RJ. An evaluation of thyroid hormone status and oxidative stress in undialyzed chronic renal failure patients. Pharmacology. 2006;50(3):279.
23. Singh S, Verma A, Aryal G, Thapa S, Khakurel S, Shrestha KJJoNHRC. Thyroid hormone profile in patients with chronic kidney disease: a single centre study. J Nepal Health Counc 2016; 34: 197-201.
24. Rajeev G, Rayappa WDSC, Vijayalakshmi R, Swathi M, Kumar SJSJoKD.. Evaluation of thyroid hormone levels in chronic kidney disease patients. Transplantation 2015;26(1):90.
25. Fan J, Yan P, Wang Y, Shen B, Ding F, Liu Y. Prevalence and clinical significance of low T3 syndrome in non-dialysis patients with chronic kidney disease. Med Sci Monit 2016; 22:1171-94.
26. Khatiwada S, Rajendra K, Gautam S, Lamsal M. Thyroid dysfunction and dyslipidemia in chronic kidney disease patients. Baral NJ Bed. 2015;15(1):65.
27. Song SH, Kwak IS, Lee DW, Kang YH, Seong EY. The prevalence of low triiodothyronine according to the stage of chronic kidney disease in subjects with a normal thyroid-stimulating hormone. Park JSJNDT 2008;24(5):1534-8.

IMJ 2023; 69(1): 29-36.