e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(8); 173-177

Original Research Article

Study of Renal Function in Hypothyroidism Patients with and without Type-2 Diabetes Mellitus: A Hospital Based Study in Govt General Hospital, Kadapa, YSR Kadapa District, Andhra Pradesh

U. Sreenivasulu[1], M. Aparna[2], P. Nagadasiah[3], B R. Shyam Prasad[4], V. Lakshmi Narasamma[5]

[1]Associate Prof, Dept of Biochemistry, GMC, Kadapa, YSR Kadapa District, Andhra Pradesh
[2]Associate Prof, Dept of Biochemistry, GMC, Kadapa, YSR Kadapa District, Andhra Pradesh
[3]Assistant Prof, Dept of Biochemistry, GMC, Kadapa, YSR Kadapa District, Andhra Pradesh
[4]Associate Prof, Dept of Biochemistry, GMC, Anantapur, Anantapur District, Andhra Pradesh
[5]Prof. & HOD, Dept of Biochemistry, GMC, Kadapa, YSR Kadapa District, Andhra Pradesh

Received: 25-06-2023 / Revised: 11-07-2023 / Accepted: 18-08-2023
Corresponding author: Dr BR Shyam Prasad
Conflict of interest: Nil

Abstract:

Introduction: Diabetes mellitus is a metabolic disease due to absolute or relative insulin deficiency. The association of thyroid dysfunction with type 2 Diabetes mellitus is widely known. Diabetic Nephropathy, a major microvascular complication of type 2 Diabetes mellitus and is an important cause of chronic kidney disease. Approximately 20%-40% of patients with diabetes progress to Diabetic kidney disease and 40% also progress to ESRD. Measurement of serum urea and creatinine are easily available tests for this purpose which can assist in detection and prevention diabetic kidney disease at an early stage and can limit the progression to end stage renal disease (ESRD). The main aim of our study is to compare the renal parameters in Hypothyroidism with typ2 Diabetes mellitus and without Diabetes mellitus.

Materials and Methods: Total of 150 subjects were taken for our study. The subjects were divided in to 3 groups, group-1: Hypothyroidism without Type 2 Diabetes mellitus patients (n= 50), Group-2: Hypothyroid patients with Type 2 Diabetes mellitus(n=50), group-3: Healthy controls(n=50) Ethical clearance: Institutional ethical committee approval was taken before commencement of study.

Sample Collection: Blood samples were collected in Govt general hospital, Kadapa, YSR Kadapa district, Andhra Pradesh. 5 ml of venous blood sample was collected from subjects in a plain tube under aseptic conditions in the morning after an overnight fast. After collection, the samples were centrifuged and serum was analysed for estimation of Thyroid hormones (T3, T4, TSH) by Chemiluminescent immunoassay- Assess 2 thyroid analyser (Beckman coulter) r. plasma glucose, serum creatinine, blood urea analysed with Semi-auto analyser.

Statistical Analysis: The data was entered and complied in an excel sheet. The data was analysed and consolidated as mean and standard deviation (SD). To analyse the statistical significance, the student t-test was performed utilizing Graph pad software. The test of the probability of less than 0.05(<0.05) was considered as significant.

Results: In the present study, the age of the subjects varied from 40-60 yrs. The mean age of the healthy controls is 44.94±2.91, Hypothyroidism without type 2 Diabetes is 45.92±3.69, Hypothyroidism with type 2 Diabetes mellitus is 46.38 ±3.98. In the present study the mean value of serumT3 and serumT4 value is low in Group-1 when compared to Group-3 ($p<0.001$, $p<0.0001$respectively). The mean serum value of TSH is significantly high in Group-1 compared to Group-3($p<0.0001$). Fasting plasma glucose mean value is high in Group-2 compare with Group-3($p<0.0001$). The mean value of serum T3, T4 is low in Group-2 compared to Group-3($P<0.0001$, $P< 0.0001$ respectively). The mean value of serum creatinine and blood urea are high in Group-2 compared to Group-3($p<0.0001$, $p<0.0001$ respectively). There is a positive Pearson correlation between Fasting Plasma glucose and serum creatinine($r=+0.31239$) and between Fasting plasma glucose and blood urea ($r = +0.1636$) in Hypothyroid patients with type-2 DM.

Discussion: Type 2 Diabetes mellitus patients were more prone to Hypothyroidism frequently. Estimation of serum creatinine and blood urea are often used to assesses the overall kidney function. Prolonged hyper glycemia which causes irretrievable damage to the nephrons of the kidney. The Serum creatinine concentration increases in hypothyroidism patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism. The main cause for increase in blood urea is Hypo thyroidism with type2 Diabetes patients is due to diminishing of glomerular filtration rate (GFR).

Conclusion: The development of Diabetic nephropathy (DN) is common in hypothyroidism patients with type 2 diabetes mellitus compared with hypothyroidism patients without type 2 Diabetes mellitus. Regular monitoring

of thyroid patients for type-2 Diabetes mellitus is very important to rule out any impact on renal function. Measurement of blood urea and serum creatinine helps in the early detection and prevention of diabetic kidney diseases and prevents the progression of end stage renal disease(ESRD).

Keywords: Hypothyroidism, Type-2 Diabetes Mellitus, Blood Urea, Serum.

Introduction

Diabetes mellitus is a metabolic disease due to absolute or relative insulin deficiency. About 10% of the total population, and about 1/5th of persons above the age of 50, suffering from this disease. It is a major cause for morbidity and mortality. The disease may be classified as following (WHO recommendation, 1999) Type- 1 Diabetes mellitus,Type2 Diabetes mellitus. Type-1 Diabetes mellitus is due to decreased insulin production and also an autoimmune basis is attributed to most of these cases. Onset is usually below 30 years of age, most common during adolescence. They are more prone to develop ketosis. About 95% of the patients belongs to Type-2 Diabetes mellitus. The disease is due to the decreased biological response to insulin, otherwise called insulin resistance. Type 2 disease is commonly seen in individuals above 40 years [1]. Diabetes is an iceberg disease. Although increase in both the prevalence and incidence of type 2 Diabetes have occurred globally. During year 2014, the number of cases of diabetes world wise is estimated to be around 422 million of these more than 90 percent are type2 Diabetes. In 2019, an estimated1.5 million people died from consequences of high blood sugar. India is a home to77million diabetics, second only to China in the world. The govt of India and diabetic retinopathy survey 2019 found11.8 per cent prevalence of diabetes in India. Males showed prevalence of 12% and females 11.7%. The long-term specific effects of diabetes include retinopathy, nephropathy, and neuropathy, among other complications. People with diabetes are also at increased risk of other diseases including heart, peripheral arterial and cerebrovascular disease, obesity and non-alcoholic fatty liver disease [2]. The association of thyroid dysfunction with type2 Diabetes mellitus is widely known. The Diabetes mellitus influences the thyroid dysfunction in two sites, first at the level of hypothalamus by controlling TSH release and second at the peripheral tissue by converting T4 into T3 [3]. The thyroid hormone exerts action on every cell of the body. Calorigenic effect or thermogenesis is the major effect of thyroid hormone. Thyroxine increases cellular metabolism [4]. The thyroid hormones directly control insulin secretion [3]. Thyroid hormone has an impact on renal tubular function and the rennin angiotensin system and is associated with hemodynamic and cardiovascular alterations that interfere with renal blood flow [3]. Subclinical hypothyroidism is the most prevalent form of thyroid dysfunction in type-2 Diabetes mellitus. Diabetic Nephropathy, a major microvascular complication of type-2 Diabetes mellitus is an important cause of chronic kidney disease. Nephropathy affects both hypothalamus-pituitary-thyroid axis and thyroid hormone peripheral metabolism [5]. Diabetic kidney is the leading cause of end-stage renal disease (ESRD) word wide. Approximately 20%-40% of patients with diabetes progress to Diabetic kidney disease and 40% also progress to ESRD [6]. Diabetic nephropathy is characterized by micro albuminuria more than 300mg (proteins specifically albumin) in a 24-hour urine collection or macro albuminuria and abnormal renal function as represented by an abnormality in serum creatinine and serum urea. In diabetic nephropathy bio-markers viz. serum urea and creatinine are known to be raised with hyper glycemia. In uncontrolled Diabetics and usually correlate with severity of kidney damage. Measurement of serum urea and creatinine are easily available tests for this purpose which can assist in detection and prevention diabetic kidney disease at an early stage and can limit the progression to end stage renal disease (ESRD) [7]. Uraemia influences the function and size of the thyroid gland, Serum TSH concentrations are usually normal or elevated in nephropathy but its response to its releasing hormone i.e., Thyroid releasing hormone is generally low [5].

The main aim of our study is to compare the renal parameters in Hypo thyroidism with type-2 Diabetes mellitus patients and without type-2 Diabetes mellitus.

Material and Methods: A total of 150 subjects were taken for our study. The subjects were divided in to 3 groups, group-1: Hypothyroidism without Type 2 Diabetes mellitus patients (n= 50), Group-2: Hypothyroid patients with Type-2 Diabetes mellitus (n=50), group-3: Healthy controls(n=50).

Inclusion criteria: The subjects with age group 40 -60 years, type 2 Diabetes mellitus patients with hypothyroidism, Hypothyroidism patients without Type2 Diabetes mellitus.

Exclusion criteria: Patients on nephrotoxic drugs, type 1 Diabetic patients, pregnant women, thyroid patients on medication, Chronic illness patients, patients on long term glucocorticoids, Hepatitis B and Hepatitis C virus patients, other known

autoimmune disease patients, subjects with age above 60yrs and below 40 excluded from study.

Ethical clearance: Institutional ethical committee approval was taken before commencement of study.

Sample collection:

Blood samples were collected in Govt general hospital, Kadapa, YSR Kadapa district, Andhra Pradesh. 5 ml of venous blood sample was collected from subjects in a plain tube under aseptic conditions in the morning after an overnight fast. After collection, the samples were centrifuged and serum was analysed for estimation of Thyroid hormones (T3, T4, TSH) by a Assess 2 thyroid analyser. plasma glucose, serum creatinine, blood urea analysed with Semi-auto analyzer. SerumT3, T4, TSH estimated by Chemiluminescent Immunoassay-Asses 2thyroid (Beckman coulter). Plasma glucose was estimated by Glucose Oxidase-Peroxidase (God-Pod) method [8], Blood urea was estimated by Urease- GLDH method [9] Serum creatinine was estimated by Jaffe's method [10].

Statistical Analysis: The data was entered and complied in an excel sheet. The data was analysed and consolidated as mean and standard deviation (SD). To analyse the statistical significance, the student t-test was performed utilizing Graph pad software. The test of the probability of less than 0.05(<0.05) was considered as significant.

Results

In the present study, the age of the subjects varied from 40-60 yrs. The mean age of the healthy controls is 44.94±2.91, Hypothyroidism without type 2 Diabetes is 45.92±3.69, Hypothyroidism with type 2 Diabetes mellitus is 46.38 ±3.98. The base line characteristics of subjects are shown in table-1.

Table 1: Base line characteristics of subjects:

Parameter	Hypothyroidism without type 2 Diabetes patients(group-1)	Hypothyroidism patients with type 2 Diabetes. (Group-2)	Healthy controls (Group-3)
No of participants	50	50	50
Age(years) Mean±	45.92±3.69	46.38±3.98	44.94±2.91
Sex (Female/ Male)	34/16	34/16	34/16

In the present study the mean value of serumT3 and serumT4 value is low in Group-1 when compared to Group-3 as shown in table-2(p<0.001,p<0.0001respectively). The mean serum value of TSH is significantly high in Group-1 compared to Group-3(p<0.0001 respectively)as shown in table-2. The mean value of serum creatinine and blood urea are high in Group-1 compared to Group-3. (P<0.0001,P<0.0001) as shown in table-2.

Table 2:

Parameter	Hypothyroidism without Type 2DM(Group-1) n=50	Healthy controls (Group-3) n=50	t-value	P-value
Fasting plasma glucose(mg/dl)	118.9±20.35	89.0±8.8	9.555	P<0.0001
Post prandial glucose (mg/dl)	148.18±14.48	121.5±10.63	10.502	P<0.0001
SerumT3 (ng/ml)	0.72±0.17	1.32±0.3	12.304	P<0.0001
SerumT4(µg/dl)	2.82±0.88	6.53±0.90	20.841	P<0.0001
Serum TSH(µIU/ml)	29.4±9.61	1.74±0.66	20.333	P<0.0001
Blood urea(mg/dl)	47.66±7.3	23.3±4.3	20.331	P<0.0001
Serum creatinine(mg/dl)	1.5±0.18	0.99±0.2	13.4025	P<0.001

The mean value of serum T3, T4 is low in Group-2 compared toGroup-3(P<0.0001, P,0.0001 respectively) as shown in table-3. The mean value of serum creatinine and blood urea are high in Group-2 compared to Group-3(p<0.0001, p<0.0001 respectively) as shown in table-3

Table 3:

Parameter	Hypothyroidism with type 2DM(Group-2) n=50	Healthy controls (Group-3) n=50	t-value	p-value
Fasting plasma glucose(mg/dl)	167.86±17.50	89.04±8.88	28.4009	p<0.0001
Post prandial plasma glucose(mg/dl)	199.4±18.53	121.5±10.63	25.7852	P<0.0001
SerumT3(ng/ml)	0.61±0.19	1.32±0.3	14.1379	P<0.0001
SerumT4(µg/dl)	2.57±0.9	6.53±0.9	21.5167	P<0.0001
Serum TSH(µIU/ml)	33.04±10.09	1.74±0.66	21.888	P<0.0001
Blood urea(mg/dl)	66.72±12.7	23.36±4.37	22.828	P<0.0001
Serum creatinine(mg/dl)	2.14±0.42	0.99±0.20	17.4805	P<0.0001

In The present study the mean value of serum creatinine and blood urea are high in Group-2 compared to Group-1 as shown in table-4

Table 4: Comparison of parameters between Hypothyroidism without Diabetes mellitus and Hypothyroidism with Diabetes mellitus

Parameters	Hypothyroidism without type-2 DM	Hypothyroidism with type-2 DM	t-value	P=value
Fasting plasma glucose (mg/dl)	118.9±20.3	167.86±17.5	12.901	P<0.0001
Post prandial plasma glucose (mg/dl)	148.18±14.48	199.4±18.5	15.4730	P<0.0001
SerumT3 (ng/ml)	0.72±0.17	0.61 ± 0.19	1.467	P=0.0066 SS
SerumT4 (µg/dl)	2.82±0.88	2.57±0.9	1.4685	P=0.1453 NS
Serum TSH (µI u/ml)	29.4±9.6	33.04±10.09	1.836	P=0.0693 Not quite statistically significant
Blood urea (mg/dl)	47.6±7.3	66.72±12.7	9.219	P<0.0001
Serum creatinine (mg/dl)	1.5±0.1	2.14±0.42	10.481	P<0.0001 ESS

NS: Not significant; SS: Statistically significant; ESS: Extremely statistically significant

There is a positive Pearson correlation between Fasting Plasma glucose and serum creatinine and between Fasting plasma glucose and blood urea in Hypothyroid patients with type-2 DM as shown in table-5.

Table 5: Pearson correlation between plasma glucose and serum creatinine, between plasma glucose and blood urea

Hypothyroid patients with type-2DM	Pearson correlation between Fasting plasma glucose and blood urea	r= +0.1636
	Pearson correlation	r=+0.31239

Discussion

Diabetes mellitus (DM) is one of the world's most important public health problems. About 90% of Diabetes patients belong to Type-2 category. Unlike type 1 diabetes mellitus, it usually affects the individual after 40 years. In these patients, unlike the case in type 1DM, insulin is not deficient, but its action is impaired (insulin resistance). β - cell dysfunction resulting in defective insulin secretion is only secondary to insulin resistance. Insulin resistance is defined as a decreased biological response to normal levels of circulating insulin [11]. Type 2 Diabetes mellitus patients were more prone to Hypothyroidism frequently [3]. Estimation of serum creatinine and blood urea are often used to assesses the overall kidney function [12]. Serum creatinine is a better indicator than urea because serum creatinine concentration is not influenced by endogenous and exogenous factors, as in the case with urea. Creatinine is an anhydride of creatine. It is formed by spontaneous cyclization of creatine or creatine phosphate. Creatine is present in the tissues (muscle, brain, blood etc.) as the high-energy compound, phosphocreatine and as free creatinine. Creatinine is excreted in urine.[13]

In the present study the mean serum creatinine value in high in Hypothyroidism with type 2Diabetes mellitus when compared to controls(P<0.0001). Our study findings are consistent with previous studies by Zhi yang eta l [14], P S Roy et al [15] P Singh et al [16]. The Serum creatinine concentration increases in hypothyroidism patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism. Serum creatinine levels may also be increased due to hypothyroid myopathy. Hypothyroidism must be considered in patients presenting with acute renal failure and elevated enzymes. The renal impairment could be due to reduced cardiac output and increased systemic and renal vasoconstriction leading to reduced renal blood and plasma flow and decreased GFR [17].

Urea is the end product of protein metabolism. Urea produced in the liver freely diffuses and is transported in the blood to kidneys and excreted. A small amount of urea enters the intestine where it is broken down to CO2 and NH3 by the bacterial enzyme urease. This ammonia is either lost in the faces or absorbed in to the blood.

In the present study the mean value of blood urea is high in Hypothyroidism patients with type 2 Diabetes patients compared to controls(p<0.0001). Our study finding consistent with previous studies by Zhi yang et al [14], P Singh et al [16].

Prolonged hyperglycaemia which causes irretrievable damage to the nephrons of the kidney. The tiny filtering units of kidneys i.e., nephrons are damaged due to high blood sugar level. As the main function of kidney is to maintain the fluid electrolyte balance, this function got impaired. The main cause for increase in blood urea is due to diminishing of glomerular filtration rate (GFR) [18]. The GFR is reversibly reduced (by about 40%) in more than 55% of adults with hypothyroidism due to several reasons. There is decreased sensitivity to β-adrenergic stimulus and decreased rennin release along with decreased angiotensin 2 and impaired renin-angiotensin-aldosterone system(RAAS)activity, resulting in loss of GFR [19]. Elevated in blood urea may also be seen after major surgery, prolonged fever, Leukaemia and bleeding disorders etc, Renal causes like acute glomerulonephritis, chronic nephritis, nephrosclerosis, polycystic kidney, Post – renal causes are mainly due to obstruction in the urinary tract (e.g. tumours, stones, enlargement of prostate gland etc.) [13]. Higher levels of blood urea

may increase insulin resistance, and supress insulin secretion and increased risk of incident of diabetes mellitus [20] End-stage renal disease (ESRD) may result because of diabetic nephropathy, contributing to evidential increase in morbidity and mortality in persons with Diabetes mellitus [15].

Conclusion:

Thyroid dysfunction causes significant changes in kidney function and most common kidney derangements associated with hypothyroidism is elevated creatinine levels. The development of Diabetic nephropathy (DN) is common in hypothyroidism patients with type2Diabets mellitus compared with hypothyroidism patients without type2Diabetes mellitus. Regular monitoring of thyroid patients for type2 Diabetes mellitus is very important to rule out any impact on renal function. Measurement of blood urea and serum creatinine helps in the early detection and prevention of diabetic kidney diseases and prevents the progression of end stage renal disease (ESRD).

References

1. DM Vasudavan, Sreekumari S, Vaidyanathan K. Textbook of biochemistry for medical students. Chapter 9;Regulation of blood glucose ,insulin and Diabetes mellitus:161-185,9th edition.
2. K.Park. Parks text book of preventive and social medicine. Chapter 6; Epidemiology of chronic non-communicable diseases and conditions; diabetes:446-450. 27th edition.
3. Datchanamurthi S, IlanchezhinT. Study of thyroid dysfunction and serum electrolytes levels in Diabetes mellitus patients. Int. J Pharm Sci Rev Res. 2022;73(1):64-68.
4. DM Vasudavan, Sreekumari S, Vaidyanathan K. Textbook of Biochemistry for medical students,9th edition. Chapter-39, Mechanisms of action of hormones: 667-690.
5. Raman Kumar Sharma, Ashwani Kumar Sharma, Sanjeev puri et al. A Comparative study of Thyroid function in patients of type2Diabets mellitus without nephropathy and Type2Diabetes mellitus with Nephropathy. Annals of International Medical and Dental Research. 2017;3(2):ME 11-ME15.
6. Yi Chen, Wen Zhang, Ningjjan wang et al. Thyroid parameters and kidney disease in Type 2 Diabetes: Results from the METAL study. Journal of Diabetes Research; 2020:1-11.
7. SA Bamanikar, AA Bamanikar ,A Arora.Study of serum urea and creatinine in diabetic and non-diabetic patients in a tertiary teaching hospital. JMR. 2016;2(1):12-15.
8. Sharp. Clin Chem Acta 1975; 40(115).
9. Kassirer J P. New Eng J Med. 1971; 285:385.
10. Young D S. Clin Chem. 1975; 21:266D.
11. Rafi MD. Textbook of Biochemistry for undergraduates, 3rd edition. Chapter 40, Hormones of the pancreas-Diabetes mellits: 522-532.
12. Dr U. Satyanarayana, Dr. Chakrapani. Biochemistry, 4th edition. Chapter 20, Organ function tests: 453-467.
13. Dr. U. Satyanarayana, Dr U. Chakrapani. Biochemistry, 4th edition. Chapter-15; Metabolism of amino acids: 330-379.
14. Zhi Yang, Peng Duan, Weihomg Li et al.The correlation between Thyroid hormone levels and the Kidney Disease Progression risk in patients with type 2 Diabetes. Diabetes Metabolic Syndrome and Obesity: Targets and Therapy 2022;15:59-67.
15. PS Roy, KVN Mallikarjuna Rao, Saphya Mukhtra et al. Evaluation of renal function and subclinical hypothyroidism in persons with type 2 Diabetes mellitus. Medpulse International Journal of Biochemistry. 2019;12(1):01-05.
16. P Singh, S Khan, R k Mittal. Assessment of thyroid dysfunction in the type 2 diabetes patients. Int j Diabetes Dev Ctries. 2014;34(4)229.
17. Kaur Sidhu G, Malek R R, Khubchandani A et al. A study of urea, creatinine and uric acid levels in Hypothyroidism patients. Int J Res Med 2016;5(2):115-118.
18. Biri SRK, Sankeerthi CH SLV, Rani T S, Gundu R et al.A Study on evaluating blood urea and serum creatinine in diabetes mellitus .Int J Clin Biochem Res. 2021;8(4):285-288.
19. BasuG, Mohapatra A.Interactions between thyroid disorders and kidney disease. Indian J Endocr Metab. 2012;16: 204-213 .
20. Yan Xie, Bowe B, Tingting Li et al. Higher blood urea nitrogen is associated with increased risk of incident diabetes mellitus. Kidney International. 2018;93:741-752.