Original Article

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eGFR Evalutation among the Hypothyroid Patients Attending at a Tertiary Center of Chattogram

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ABSTRACT

Background: *Hypothyroidism is a prevalent endocrine illness that affects people all over the world. The modulation of renal hemodynamics and basal metabolic rate is disrupted in hypothyroidism. The kidney is generally involved in thyroid hormone metabolism, breakdown and excretion. Chronic renal hypoperfusion affects the hypothalamic-pituitary-thyroid axis, resulting in low circulating thyroid hormone levels, changed peripheral hormone metabolism, decreased tissue thyroid hormone content and altered thyroid iodine storage. Recent research has linked an increased risk of hypothyroidism to a decreased estimated Glomerular Filtration Rate (eGFR). The purpose of the study is to determine the association between eGFR with hypothyroidism in a tertiary care hospital of Chattogram.*

Materials and methods: *A cross sectional study was done during July 2022 to June 2023 including 100 diagnosed hypothyroidism cases attending in Chittagong Medical College Hospital. Serum Thyroid Stimulating Hormone (TSH) serum free thyroxine (FT4) serum creatinine, and blood urea were measured. The estimated glomerular filtration rate (eGFR) were determined. The result were analysed using SPSS version 25.*

Results: *The mean age was 42.76±10.18 years with 93% female. Most of the patients (92%) were in a subclinical hypothyroid state and 8% were in an overt hypothyroid state. The mean ±SD serum creatinine levels and urea levels were 0.8±0.2mg/dl and 25.4±6.5 mg/dl, respectively. The mean eGFR was 75.36±7.54 ml/min/1.73 m^2. There was a significant decrease in mean eGFR in the < 60 ml/min/1.73m^2 group among the study population. There was a significant association between decreased eGFR and hypothyroidism. Serum TSH had significantly shown a negative correlation with eGFR. Serum TSH level had a significant positive correlation with serum creatinine (r=0.56, p<0.05) and serum urea (r=0.25, p<0.05). There was a significant eGFR difference between subclinical hypothyroidism and overt hypothyroidism.*

Conclusion: *It can be concluded from this study that the hypothyroidism was significantly correlated with decreased eGFR.*

Key words: Creatinine; eGFR; Hypothyroid; Serum TSH.

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Introduction

Endocrine diseases have a considerable impact on public health from an epidemiological point of view. Because they may cause long-term disability, alteration of the quality-of-life of the affected patients and the fifth leading cause of death. The study evaluated the prevalence of different disorders of endocrine interest in the world and found that thyroid disorders were among the most common endocrine diseases. Hypothyroidism is one such thyroid disorder that can lead to a range of symptoms such as fatigue, weight gain, constipation, dry skin, hair loss and more.[1] The actual burden of thyroid dysfunction in Bangladesh is largely unknown though it is believed that 20% of our general population has been suffering from any thyroid disorder.[2] In a study conducted by Paul et al. the overall occurrence of thyroid disease was 20.43%; the spectrum of thyroid disorders showed the highest incidence of diffuse goiter (7.35%) followed by subclinical hypothyroidism (6.59%) hypothyroidism (4.97%) hyperthyroidism (0.86%) and subclinical hyperthyroidism (0.65%).[3]

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Thyroid Hormones (TH) regulate the renal hemodynamics and basal metabolic rate of most cells. The thyroid gland synthesizes and releases triiodothyronine (T3) and thyroxine (T4) which represent the only iodine containing hormones in the vertebrates. T3 is the biologically active thyroid hormone. These hormones are required for the normal growth, development and function of nearly all tissues, with major effects on oxygen consumption and metabolic rate.[4] Acute and chronic renal illness has been linked to major impacts on the hypothalamus-pituitary-thyroid axis. Thyroid-Stimulating Hormone (TSH) levels in Chronic Kidney Disease (CKD) may be normal or raised, but there is a diminished response to Thyrotropin-Releasing Hormone (TRH). There is a change in circadian rhythm and activity, indicating hypophyseal abnormalities. Thyroid hormone replacement therapy improves kidney function in patients with subclinical or overt hypothyroidism, according to observational designs or small randomized trials. However, no large-scale, long-term randomized trial has been conducted to more conclusively establish the potential existence and directionality of a causal relationship between thyroid and kidney function.[5] On the other hand, it has been discovered that hypothyroidism and subclinical hypothyroidism cause the prevalence of Chronic Kidney Disease (CKD) to rise with time. Furthermore, low free triiodothyronine (FT3) levels even within the normal reference range have been linked to greater risks of developing Chronic Kidney Disease (CKD).[6] Despite being within the clinically normal reference range, low thyroid hormone levels have been associated with reduced eGFR. Additionally, TSH within the normal range has been consistently and independently linked to elevated urine albumin/creatinine ratio and reduced GFR in CKD. Plasma creatinine levels and eGFR were examined before Thyroid Hormone Replacement Therapy (THRT). They have found that after restoring euthyroidism in a short trial with 37 hypothyroid and 14 hyperthyroid individuals; THRT dramatically improved renal function in previously hypothyroid patients[12]. Furthermore, it has been demonstrated that individuals with CKD and subclinical hypothyroidism benefit from thyroid hormone replacement treatment by maintaining renal function and delaying the loss of eGFR.[7]

Materials and methods

This was a descriptive type cross-sectional study conducted in Chittagong Medical College Hospital. 100 hypothyroid diagnosed cases were included in the study by convenience sampling. Cases were selected from the Outpatient Department of Medicine and Department of Endocrinology at Chittagong Medical College Hospital. A predesigned case record form was used to record relevant data. All the data were processed and analyzed using IBM-SPSS (Statistical Package for Social Science) v 25.0 for Windows. p value < 0.05 considered to be statistically significant. The chi-square test and independent sample t-test have been applied whenever necessary to see the statistical significance among TSH and eGFR. The Association of TSH and eGFR was determined by chi (χ^2) square test. To test the correlation among TSH, FT4 and eGFR done by Pearson's correlation coefficient. The frequency distribution of different variables like age, sex was summarized and presented in the form of tables and charts.

Results

Table I Distribution of gender among hypothyroidism patients based on age (n=100)

Age Group	Male	Female	%
<20	1	3	4.0
21-30	1	9	10.0
31-40	1	21	22.0
41-50	3	39	42.0
51-60	1	21	22.0
Total	7	93	100.0

Mean age : 42.76 ± 10.18

The most frequent age group was 41-50 years, 42% of the patients.

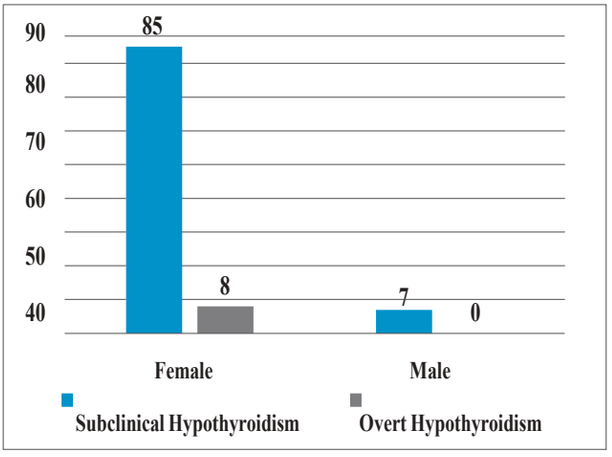

Figure 1 Gender distribution of hypothyroid patients (n=100)

Among Male patients, the number of subclinical hypothyroidism was 7%. Among
Female patients, 85 were subclinical hypothyroidism and 08 were overt hypothyroidism.

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Table II Comparison of serum creatinine and blood urea levels between subclinical hypothyroid and overt hypothyroid patients (n=100)

Renal biochemical parameters	Subclinical hypothyroid (n=92)	Overt hypothyroid (n=08)
Serum creatinine, mg/dl	0.8 ± 0.2	1.1 ± 0.2
Blood urea, mg/dl	24.8 ± 6.0	31.4 ± 9.2

The above table shows that mean serum creatinine and blood urea levels were higher in patients with overt hypothyroidism than the patients with subclinical hypothyroidism.

Table III Age and eGFR differences between male and female patients (n=100)

Variable	Male (7)	Female (93)	p value
Age (Years)	41.43±10.8o	42.86±10.19	t=0.34 at 5% level CV=1.67 (N.S)
eGFR (ml/min/1.73m^2)	93.89±8.24	73.97±13.66	t=5.82 CV at p.01=2.62 So, significant

The mean age of male was 41.43±10.80 years and female was 42.86±10.19 years. Difference not significant (p .05)

There is a significant mean difference in eGFR between male and female among the study population. (t=5.82, significant at p.01)

Table IV The mean difference of serum FT4, TSH and eGFR between subclinical hypothyroidism and overt hypothyroidism (n=100)

Subclinical hypothyroidism Serum FT4 (Mean±SD)	Overt hypothyroidism Serum FT4 (Mean±SD)
16.42±0.29	9.24±0.18
p value < 0.001	
Subclinical hypothyroidism Serum TSH (Mean±SD)	**Overt hypothyroidism Serum TSH (Mean±SD)**
7.71±0.31	25.28±1.70
p value < 0.001	
Subclinical hypothyroidism eGFR ml/min/1.73m^2	**Overt hypothyroidism eGFR ml/min/1.73m^2**
Mean±SD 77.34±12.96	Mean±SD 53.23±10.34
p value < 0.001	

The above table shows that there is significant mean difference between FT4, TSH and eGFR among the patients of subclinical hypothyroidism and overt hypothyroidism.

Table V Correlation between different study variables (n=100)

Variable	r	p
Serum TSH and serum Creatinine	+0.56*	< 0.05*
Serum TSH and eGFR	-0.53*	< 0.05*
Serum TSH and blood urea	+0.25*	< 0.05*
Serum TSH and Age	+0.17	> 0.05
Serum FT4 and serum Creatinine	-0.34*	< 0.05*
Serum FT4 and eGFR	+0.39	< 0.05*
Serum FT4 and blood urea	-0.13	> 0.05
Serum FT4 and Age	-0.006	> 0.05

There is a significant positive correlation between serum TSH and serum creatinine and blood urea and a significant negative correlation between serum TSH and eGFR. There is also a significant negative correlation between serum FT_4 and serum creatinine.

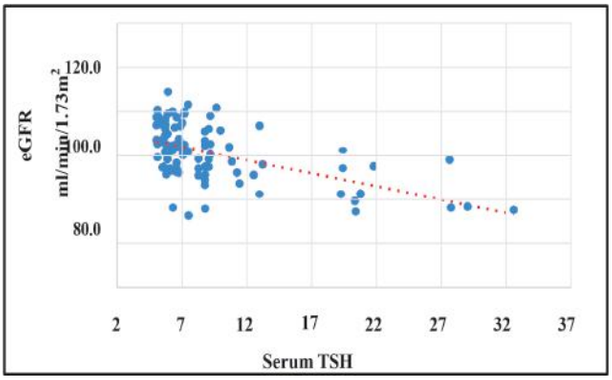

Figure 2 Scatter diagram with trendline between serum TSH and eGFR(n=100)

It is depicted from the above figure that eGFR was decreasing as the serum TSH increased.

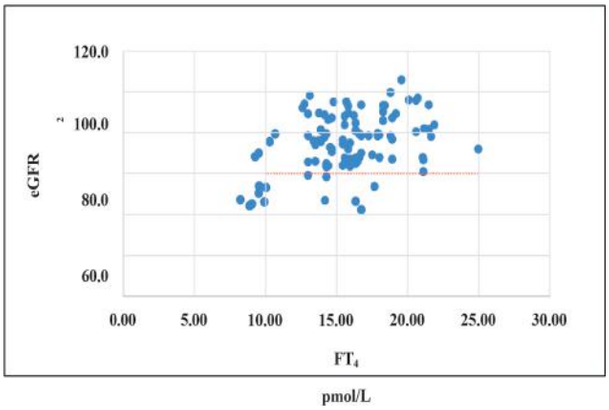

Figure 3 Scatter diagram with trendline between serum FT4 and eGFR (n=100)

It is observed that the trendline for eGFR was decreasing as the serum FT_4 value decreased.

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Discussion

In the present study, the age range was between 18-60 years with a mean age of 42.76 ± 10.18 years with [p=> 0.05] which is not significantly correlated. The most frequent age group was 41-50 years with 42% of the patients. 4 patients were in ≤20 years age group (4%). The age distribution of the current study agreed with a previous study conducted in another tertiary level center in Dhaka, where the majority of the diagnosed hypothyroid patients were in 31- 40 years of age group (37.5%).[8] This study observed that TSH levels were positively correlated with age up to 60 years. This phenomenon is observed by Saha.[9] The mean TSH in this study was 9.19±0.56, such an increased value of TSH was seen in other similar studies.[10] The frequency of subclinical hypothyroidism (93) in female was higher than in male (07) among the study population. There is a significant difference in eGFR between male subclinical hypothyroidism and female subclinical hypothyroidism and between subclinical hypothyroidism and overt hypothyroidism among the present study population, which agreed with the study of Patil1.[11] There is a significant difference in serum TSH and serum FT_4 between subclinical hypothyroidism and overt hypothyroidism. This observation is similar to another study.[12] In the present study, the mean ±SD serum creatinine level was 0.87±0.01 mg/dl. The mean eGFR was 75.36±7.54 ml/min/1.73 m^2 and 10% of the patients had eGFR below 60 ml/min/1.73 m^2.Montenegro observed that all their hypothyroid patients had decreased eGFR and 22 patients had increased serum creatinine levels out of 44 patients.[13] In this study, it was seen that there is a positive correlation between serum TSH and serum creatinine [r=+0.56, p=<0.05], Though the the mean creatinine is 0.8 ± 0.2, which is within normal range. Serum TSH and blood urea [r=+0.25, p=<0.05], relation was significant. Though the mean urea was 24.8 ± 6.0, which is within normal range. There is also a significant negative correlation between serum TSH and eGFR [r=-0.53, P=<0.05], serum FT_4 and serum creatinine [r=- 0.34, p=<0.05] among the study population. It is also seen that there is a significant association between decreased eGFR and overt hypothyroidism; with chi square value
40.82. Serum TSH level had significant positive correlation with serum creatinine in the present study and a reverse trend was observed regarding the relation between TSH and eGFR. In the study of Patil, a significant correlation between TSH, creatinine, and eGFR was found in overt hypothyroid group only.[11] In the study of Saha, eGFR was significantly correlated with TSH values.[9] Serum urea demonstrates a huge negative connection with serum TSH while serum creatinine indicates critical negative connection serum T4 and serum TSH in another study of Singh et al. and the relationship between TSH and serum creatinine level persist after adjustment for other related variables such as age, BMI, blood pressure.[14] The relationship between hypothyroid and a deterioration in renal function has been studied using a variety of epidemiological data and clinical trial data. An expanding amount of cross- sectional research indicates that both overt and subclinical hypothyroidism is linked to decreased eGFR and a higher risk of CKD. According to Zhang, people with subclinical hypothyroidism have a higher risk of developing CKD when their TSH and FT4 values were above and below normal, respectively.[15] This study has found a significant mean difference of eGFR in the < 60 ml/min/1.73m^2 group among the study population, which agreed with the study of Wang.[16]

Limitation

The sample size is small and collected from single center which do not reflect the condition of the whole country. Cross sectional type of the study design is not suitable to determine the association between thyroid dysfunction and renal dysfunction. Absence of a healthy control group was another limitation of the present study.

Conclusion

This cross sectional study evaluates the association between increased serum TSH and decreased eGFR in hypothyroid patients. The TSH values may be used to predict the lower kidney function in Hypothyroidism. The female preponderance of subclinical hypothyroidism is also observed than overt hypothyroidism.

Recommendation

The renal function should be regularly monitored in hypothyroid patients. However, future large- scale prospective studies are needed to determine the potential adverse effects of hypothyroidism on renal function.

Disclosure

All the authors declared no conflicts of interest.

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