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Original Article

DERANGEMENT OF SERUM BIOCHEMICAL MARKERS OF RENAL FUNCTIONS IN HYPERTHYROID NON-PREGNANTWOMEN

"A HOSPITAL BASED CROSS SECTIONAL STUDY FROM KHYBERPAKHTUN KHAWA PROVINCE OF NORTHERN PAKISTAN"

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ABSTRACT

Aim and objective: This hospital based cross sectional study was carried out to study the effect of hyperthyroidism on the serum biochemical markers of renal function in non-pregnant women in Khyber Pakhtunkhaw. **Background**: Thyroid Hormones (TH) play a very important role in growth, development and functions of the kidney. This present cross-sectional study was carried out to generate a data about thyroidal hyper function and its ill effects on the biochemical markers of renal functions in Non-pregnant Women (NPW) of Khyber Pakhtunkhwa in Northern Pakistan. **Material and Methods**: The study was conducted on 163 non-pregnant women in the age group of 18-75 attending various outpatient departments in Khyber Teaching Hospital (KTH) of Khyber pakhtunkhaw. Serum T_3 and T_4 analysis was performed using competitive ELISA technique and serum TSH was performed using sandwich ELISA technique. Serum urea was measured by kinetic method and Serum creatinine by modified Jaffe method.**Results**: Mean serum creatinine was highest in normal (N) group (1.47±1.25 mg/dl) as compared to Overtly Hyperthyroid (OH) (1.29±0.01 mg/dl) and sub clinically Hyperthyroid (SH) group (1.34±0.15 mg/dl). Mean Serum Urea level was found elevated in OH (35.35±1.75 mg/dl) and SH (32.98±1.63 mg/dl) as compared to N group (32.60±1.22 mg/dl). Serum creatinine showed positive relation with TSH, in all the study groups, negative with T_3 in N group, OH group and positive in SH group. Serum creatinine showed a significant positive correlation with TSH in OH group (p= 0.05). Serum creatinine showed a significant negative correlation with T_3 in N group (p= 0.05). No significant correlation with T_4 was found either for creatinine or Urea in any of the study groups.

Key words: Hyperthyroidism, Creatinine, Urea, Non-Pregnant Women, biochemical markers.

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INTRODUCTION

The interactions between renal and thyroid functions are well known for

many years[1]. Thyroid Hormones (TH) play a very important role in the growth, development, and functions of the kidney[2]. It has been found that hyperthyroidism increases the kidney-to-body weight ratio [3].The kidney also plays a key role in the regulation, metabolism and elimination of Thyroid Hormone (TH) [4]. Thyroid dysfunction produces significant changes in renal function. Both hyperthyroidism and hypothyroidism affect renal blood flow, tubular function, Glomerulus Filtration Rate (GFR), electrolyte pump functions, electrolytes homeostasis, and kidney structure [4].The common kidney complications linked with thyroid dysfunction includes elevation of serum creatinine levels, Renal Plasma Flow (RPF), decrease in GFR and disruption of the capacity to excrete free water and hypernatremia in both adults and children [5-7]. Some authors have also reported an increase of serum creatinine in subclinical hypothyroidism [8].

Hyperthyroidism or thyrotoxicosis results in an increase of GFR and RPF and decrease of serum creatinine levels [9]. These changes are normalized after appropriate treatment [4]. The decrease in serum creatinine has also been reported in subclinical hyperthyroidism [8].The different types of kidney diseases can be associated with various disorders of thyroid function.

Both hypothyroidism[10]and hyperthyroidism[11] can coincide with different forms of glomerular disease. The more frequent form is membranous glomerulopathy associated with Nephrotic Syndrome (NS) [12]. Thyroid dysfunction has been reported to be associated with IgA glomerulonephritis [13].

Thyroidal dysfunctions are more prevalent in females and its adverse effects in pregnant females are well established. Hyperthyroidism is10 times more common in women than in men [14]. It has been found to occur in around 2.5% of normal pregnancies [15]. According to a WHO report on the nutritional value of vitamins and minerals, the prevalence of goiter in Pregnant Women (PW) is 22.2% while in Non-pregnant Women (NPW) is 20.9 % respectively.

The data about the prevalence and ill effects of hyperthyroidism on renal function in Non-pregnant Women (NPW) is limited especially in south Asia in general and Pakistan in particular. The purpose of the present study is to generate a data about the prevalence rate of hyperthyroidism in non-pregnant women Khyber pakhtunkhaw and to study its ill effects on the biochemical markers of renal functions.

METHODOLOGY

Study design/ Study site

This cross sectional study was carried out from 01 March 2014 to 31 March 2015 in Khyber Teaching Hospital (KTH), a tertiary care hospital in Khyber Pakhtun Khwa province of Northern Pakistan. The study was approved by the ethical committee of the Khyber Teaching Hospital(KTH), a tertiary care hospital in Khyber Pakhtunkhwa province of Northern Pakistan through its letter no 21876/KTH/ P.S.

Khyber Teaching Hospital (KTH) is a state of the art tertiary care hospital located in Peshawar city, in Northern Pakistan. It has 18 specialties with 600 active beds catering to the needs of almost one million populations.

The total no of patients visiting various outpatient departments during this period were 539968. Out of these 281,311 were females and 258,657 males. The total referral cases from these departments for thyroid screening were 15667. 3010 were found to be newly diagnosed cases of thyroidal dysfunctions. 2303 were females and 707 males. The ratio of female and male was 3.26:1. Out of total female patients, 605 were below 18 years, 442 were pregnant and 1147 were sufferings from various diseases like kidney, liver, bone, heart ailment, diabetes and hence were excluded from the study. The study group comprises of 109 non pregnant hyper thyroid women. Normal (N) group consisting of 54 non pregnant women were recruited from the local area in Peshawar city. Informed consent was sought from the patients through a well-designed data entry form. All human dignity was respected in accordance with international norms involving human as an experimental subjects. Information's regarding age; BMI, medical history etc were collected in the data entry form. 5 ml of fasting venous blood sample was collected from each patient. Serum was divided into two part- one part was used for thyroid function tests by Elisa techniques and the other was immediately analyzed for the determination of Serum creatinine and Serum Urea using Standard protocols.

Thyroid function tests

Serum TSH, T_4 and T_3 were assayed using ELISA kits obtained from Biocheck, Inc catalog Nunber: BC-1001, BC-1007 and BC-1005 respectively. Serum T_3 and T_4

were performed using competitive ELISA technique [16, 17] and serum TSH was performed using sandwich ELISA technique [18]. The normal ranges for TSH, T_4 and T_3 values were 0.4- 6.0 ?IU/ml, 4.8-12.0 ?g/dl, and 0.6-1.85 ng/ml respectively.

Renal function tests

Serum urea and creatinine levels were determined on autoanalyser (Erbamannhein chemistry autoanalyser, Germany) using standard Erba kits. Serum urea was measured by kinetic UVmethod [19] and Serum creatinine by modified Jaffe method [20]. The normal ranges were 05-45 mg/dl for Urea and 0.5-1.5 mg/dl for creatinine.

After conducting thyroid function tests, subjects having euthyroid state (n=54, TSH?6.0?IU/ml, normal T_3 and T_4 levels) were taken as controls (N). Hyperthyroid patients (n=109) constituted the study group. These patients were further sub divided into Sub clinicaly hyperthyroid(SH) (n=51); TSH ? 6.1 ?IU/ml with normal T_4 and T_3 levels) and Overtly hyperthyroid(OH) (n=58) with TSH ? 6.0 ?IU/ml and/ or abnormally high T_4(above 4.8 ?g/dl) and T_3(above 0.6ng/ml) levels.

Statistical analysis

Statistical analysis was carried out using SPSS for windows 21.0 software (SPSS Inc.,Chicago, IL, USA) and Microsoft Excel. Values were reported as mean ± standard error of mean. Pearson's correlation was applied to test for association between continuous variables. A two-tailed p value<0.05 was considered statistically significant.

RESULTS

Base line characteristic of the study group

The study group and the control group were age matched 163 Non- Pregnant Women (NPW). The mean age of patients in the control group (N) was 42.15 ± 1.86 years, 49.74±1.62years for Overtly Hyperthyroid (OH) and 48.94±1.87 years for the Sub clinically Hyperthyroid (SH).The control group were 54, of which 61.11%(33) were Menopausal (M, age below 45 years), 18.52%(10) were Early Post-Menopausal (EPM, age 45-50 years) and 20.37% (11) were Late Post-Menopausal (LPM, age above 50 years). Similarly the %age of M, EPM and LPM in the OH (58) and SH (51) were 34.48% (20), 27.58% (16),37.93%(22)and 43.14% (22),07.84%(04), 49.07% (25) respectively.

Comparison of the biochemical markers of thyroid function and renal function of the studygroup

The values of thyroid hormones and biochemical markers of renal function are presented in table no1. The mean serum level of TSH was found to be lowest in OH group (0.17±0.01µIU/ ml) and highest in the N group (2.38± 0.49µIU/ ml).Serum T_3 level was highest in OH group (2.37±0.01 ng/ml) and lowest in SH group (1.64±0.04 ng/ml). Highest serum T_4 level was found for OH group (12.07±0.46 µg/ dl) and lowest in SH group (8.16±0.24) µg/ dl).Mean serum creatinine was highest in N group (1.47±1.25 mg/dl) as compared to OH (1.29±0.01 mg/dl) and SH group (1.34±0.15 mg/dl). Serum Urea level was found elevated in OH(35.35±1.75 mg/dl) and SH (32.98±1.63 mg/dl) as

TABLE 1:
THYROID PROFILE AND RENAL FUNCTION BIOCHEMICAL MARKERS IN NON-PREGNANT WOMEN

S no	Group ID	Frequency(n)	Thyroid profile markers			Renal markers	
			TSH	T_3	T_4	S.Creatinne	S.Urea
1	N	54	2.38±0.49	1.68±0.05	8.50±1.59	1.47±1.25	32.60±1.22
2	OH	58	0.17±0.01	2.37±0.01	12.07±0.46	1.29±0.01	35.35±1.75
3	SH	51	0.18±0.01	1.64±0.04	8.16±0.24	1.34±0.15	32.98±1.63

N: Normal, OH: Overtly hyperthyroid, SH: Sub clinically hyperthyroid
TSH: Thyroid Stimulating Hormone, T_3 :Triiodothyronine, T_4 : Tetraiodothyronine

TABLE 2:
Regression analysis of thyroid profile with BMI of the study groups

Parameter	Thyroid profile	N		OH		SH	
		R	Sig	R	Sig	R	Sig
BMI	TSH	0.35	0.33	5.15	0.18	-7.03	0.05
	T_3	-0.12	0.93	0.60	0.27	0.64	0.36
	T_4	-0.80	0.01	-0.30	0.01	-0.11	0.46

TABLE 3:
Regression analysis of thyroid profile with renal markers in the Normal group (N)

S no	Constant	Variable			
		S.Creatinine		S.Urea	
		R	Significance	R	Significance
1	TSH	0.12	0.38	0.03	0.98
2	T_3	-0.90	0.06	0.86	0.81
2	T_4	0.15	0.16	-0.92	0.26

TABLE 4:
Regression analysis of thyroid profile with renal markers in the Overtlyhyperthyroid group (OH)

S no	Constant	Variable			
		S.Creatinine		S.Urea	
1	TSH	1.67	0.08	8.83	0.66
2	T_3	-0.004	0.98	-3.91	0.16s
3	T_4	-0.01	0.71	-0.02	0.97

TABLE 5:
Regression analysis of thyroid profile with renal markers in the subclinically hyperthyroid group(SH)

S no	Constant	Variable			
		S.Creatinine		S.Urea	
		R	Significance	R	Significance
1	TSH	2.58	0.09	0.75	0.50
2	T_3	0.13	0.67	-4.66	0.88
3	T_4	0.04	0.59	-0.41	0.05

TABLE 6:
Correlation analysis of renal markers with TSH in the study groups

Parameter	Group ID	Biochemical markers of renal function			
		S.Creatinine		S.Urea	
		R	P	r	P
TSH	N	0.19	0.17	0.004	0.98
	OH	0.25*	0.05	0.11	0.41
	SH	0.23	0.08	-0.001	0.10

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

TABLE 7:
Correlation analysis of renal markers with T_3 in the study groups

Parameter	Group ID	Biochemical markers of renal function			
		S.Creatinine		S.Urea	
		R	P	r	P
T_3	N	-0.27*	0.05	0.004	0.98
	OH	-0.08	0.55	-0.22	0.91
	SH	0.10	0.45	-0.23	0.09

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

TABLE 8:
Correlation analysis of renal markers with T_4 in the study groups

Parameter	Group ID	Biochemical markers of renal function			
		S.Creatinine		S.Urea	
		R	P	r	P
T_4	N	0.13	0.33	-0.16	0.26
	OH	-0.11	0.44	-0.10	0.44
	SH	0.09	0.51	-0.15	0.25

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

compared to N group (32.60±1.22 mg/dl).

Regression analysis of the study group

The regression analysis of thyroid profile with BMI and renal markers of all the three study groups are presented in table no2, 3, 4 and 5.

BMI was found to be positively related with TSH and negativelyrelated with T_3 and T_4 inN group. BMI showed negative relation with T_4 in OH and SH groups. Serum creatinine showed positive relation with TSH, in all the study groups, negative relation with T_3 in the N group and OH and positive in SH group. It showed positive relation with T_4 in N and SH and negative in OH group. Serum urea showed positive relation with TSH in all groups, with T_3 in N and negative in SH and OH groups. Serum urea showed negative relation with T_4in allgroups.

Correlation analysis

The Pearson's correlations of biochemical markers of renal function with the different components of thyroid function tests were evaluated. Serum creatinine showed a significant positive correlation with TSH in the OH group (p= 0.05). Serum creatinine showed a significant negative correlation with T3 in the N group (p= 0.05). No significant correlation with T_4 was found either for creatinine or Urea in any of the study groups.

DISCUSSION

Kidney and thyroid functions and dysfunctions are interrelated through complex mechanisms.

From a clinical perspective, in patients with kidney disease, it is sufficient to use thyroid function tests used in the routine clinical laboratory. However, to avoid confusion in diagnosis, it is usually necessary to know the effects of hypothyroidism and hyperthyroidism on kidney function, as well as the changes in thyroid hormone level.

Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Excessive levels of thyroid hormone (TH) level result in an increase in Glomerular Filtration Rate (GFR) and Renal Plasma Flow (RPF). The association of different types of glomerulopathies with both hyper- and hypo function of the thyroid has been reported. Nephrotic Syndrome (NS) is accompanied bychanges in the concentrations of TH due to loss of protein in the urine. Some authors have reported associations between thyroid cancer and kidney tumors and each of these organs can develop metastases into the other. Data from recent research show that TH, especially T_3, can be considered as a marker for survival in patients with kidney disease.

Thispresent cross-sectional study was carried out to study the prevalence of hyperthyroidism in and its ill effects on the biochemical markers of renal functions in Non-pregnant Women (NPW) of Khyber Pakhtunkhwa in Northern Pakistan. Mean serum creatininewas found to be highest in N group as compared to OH and SH group. Serum Urea level was found elevated in OH and SH as compared to N group. Other similar studies have reported that hyperthyroidism or thyrotoxicosis results in an increase of GFR and RPF and decrease of serum creatinine levels [9]. These changes are supposed to be normalized after appropriate treatment [4]. The decrease in serum creatininehas alsobeen reported in subclinical hyperthyroidism [8].The different types of kidney diseases can be associated with various disorders of thyroid function. We found in our studythat BMI was positively related with TSH and negatively related with T_3 and T_4 in N group. BMI showed negative relation with T_4 in OH and SH groups. Serum creatinine showed positive relation with TSH, in all the study groups, negative relation with T_3 in the N group and OH and positive in SH group. Similar results have been reported by other studies. Serum creatinine showed a significant positive correlation with TSH in the OH group (p= 0.05). Serum creatinine showed a significant negative correlation with T_3 in the N group (p= 0.05). No significant correlation with T_4 was found either for creatinine or Urea in any of the study groups [21]. The strong points about this present study is that no such study has been carried out in this part of Pakistan, although there are a number of studies from other parts of the word reporting such effects of thyroidal dysfunctions on renal functions[21] .The study has got a no of limitations which could not be minimized despite our best efforts. The most important limitation was the sociocultural barriers, hindering the collection of data from the patients, regarding family medical history, medications and economic conditions. Other renal markers like Cystatin C, ?- trace protein and urinary Albumin which are considered better renal markers were not measured due lack of laboratory facilities and financial constraints. Lastly the study was carried out only in one Centre involving only 163 Non Pregnant Women and hence cannot be generalized. Further studies are required involving larger populations for better

results.

CONCLUSION:

There is a complex interaction between thyroid and kidney, thus it is important to look for both the possibilities in the diagnosis of clinical condition affecting either organ.

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Authors contribution:
* Write the research paper ** Supervise *** Assist in lab working and statistics

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