Original Article

Effect of Hypothyroidism on Renal Function

Serum Biochemical Markers of Renal Functions May Not Be Impaired in Newly Diagnosed Non-Pregnant Hypothyroid Women

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ABSTRACT

Objective: Thyroid hypo function is known to cause renal impairment. The present Cross-Sectional study was conducted to investigate the effects of thyroid hypo function on the Serum Biochemical Markers (SBM) of Renal Function (RF) in Non-pregnant hypothyroid women.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Khyber Teaching Hospital (KTH) a tertiary care hospital in KhyberPakhtun Khwa province of Northern Pakistan from 01 March 2014 to 31 March 2015

Materials and Methods: Thyroid profile status (T_3, T_4 and TSH levels) was determined for the selected 150 patients. On the basis of Thyroid profile, patients were divided into three groups as Normal (N) (n=54), Sub-clinically hypothyroid (Sh) (n=48) and overtly hypothyroid (Oh) (n=48). Biochemical analysis for Serum Creatinine (S.C) and Serum Urea (S.U) were conducted in all the patients and the data was analyzed statistically, using SPSS version 21.

Results: A minor decrease in the serum creatinin level in the Oh (1.10mg/dl) and Sh group (1.18 mg/dl) was found as compared to N group (1.47mg/ dl). Serum urea was found to be slightly decreased in the Sh group (23.22 mg/dl) as compared to N group (32.60mg/dl) and Oh group (30.11mg/dl). A very significant positive correlation was found between Serum creatinine and T_3 in the Sh group (p= 0.005) and significant negative correlation with T_3 in the N group (p= 0.05).Urea was significantly negatively correlated with TSH in Sh group (p= 0.05).

Conclusion: Hypothyroidism may not affect renal functions in non-pregnant women in Northern areas of Pakistan.

Key Words: Renal Markers; Thyroidal dysfunctions, Creatinine, Urea, Non-Pregnant Women.

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INTRODUCTION

Iodine is one of the important trace elements and is necessary for the biosynthesis of thyroid hormones and normal activity of the body[1]. Iodine deficiency disorder (IDD) causes hypothyroidism which impairs reproduction, causes goiter in all age groups, abortions, cretinism and neurological complications [2, 3]. Disorders of the Thyroid glands are the most prevalent disorders of the endocrine glands in the world, especially in Asia [4]. In thyroidal dysfunction, the sensitive biochemical marker is Thyroid Stimulating Hormone (TSH) which is highly decreased in hyperthyroidism (<0.05mIU/l) [2] and is elevated in hypothyroidism [3].These thyroidal dysfunctions have serious ill effects on renal functions.

It has been found that Thyroidal dysfunctions disturb the kidney to body weight ratio [5].

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It has been reported that children with Congenital Hypothyroidism (CH) have a high prevalence of congenital kidney abnormalities [6]. The kidney is also believed to play a significant role in the metabolism and removal of thyroid hormones from the body [7].

Thyroidal dysfunctions are more prevalent in females and its adverse effects in pregnant females are well established. Hypothyroidism is 10 time more prevalent in women as compared to men [8]. Its prevalence rate is around 2.5% in normal pregnant women [9].

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. 2.5 billion Populations are suffering globally from iodine deficiency, out of which 313 million live in the South-Eastern Asian countries including Pakistan[10].

The northern areas of Pakistan are well known to be endemic iodine deficient. The goiter prevalence is found to be 55% in plains to 80-90% in the northern mountainous region [11, 12].

The data about ill effects of hypothyroidism in Non-Pregnant Women (NPW) is limited especially in South Asia in general and Pakistan in particular.

The objectives of the present Cross-Sectional study is to generate a data about the thyroidal hypo function and its ill effects on the biochemical markers of renal function in Non-Pregnant Women (NPW) of Khyber Pakhtunkhawa in northern Pakistan

MATERIALS AND METHODS

Study populations: This hospital based cross sectional study was conducted 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 conducted on 150 Non- pregnant Women of age group 18 to 75. Informed consent was sought from the patient/attendant. All ethical principles were observed in accordance with resolution 196/96 on research involving human subjects. The study was approved by the Ethical Committee of the Khyber Teaching Hospital (KTH), a tertiary care hospital in Khyber Pakhtunkhawa province of Northern Pakistan through its letter no 21876/KTH/ P.S. KTH is a tertiary care hospital in Peshawar city of Northern Pakistan having about 600 active beds in 18 specialties like Cardiology, ENT, Nephrology, medicine, Gynae, Dental, Orthopedic, Plastic surgery, Oncology etc. 5 ml of fresh venous blood was taken from each patient. It was divided into two portions- one portion was used for the determination of thyroid profile markers by Elisa methods and the other portion was used for the determination of Serum creatinine and Urea using Standard protocols.

Thyroid profile markers determination: Thyroid profile markers (Serum TSH, T_4 and T_3) were determined using ELISA kits obtained from Biocheck, Inc. catalog Number: BC-1001, BC-1007 and BC-1005 respectively on Dia 710 micro plate reader (Made in Australia). Serum Triiodothyronine(T_3) and Tetraiodothyronine(T_4) were determined using Competitive ELISA methods [13, 14] and TSH was analyzed by Sandwich ELISA method [15]. The normal values for TSH, T_4 and T_3 were 0.4- 6.0 µ IU/ml, 4.8-12.0 µg/dl, and 0.6-1.85 ng /ml respectively.

Renal markers determination: Serum Urea and Creatinine levels were determined on autoanalyser (Erbamannhein chemistry autoanalyser, Germany) by using standard Erba kits. Serum Urea was determined by Kinetic Method [16] and Serum creatinine by modified Jaffe method [17]. The normal ranges were 05-45 mg/dl for Urea and 0.5-1.5 mg/dl for creatinine.

After the determination of thyroid profile status, patients having normal thyroid profile (n=54, TSH≤6.0, normal T_3 and T_4 levels) were taken as controls. While the hypothyroid patients (n=96) constituted the Study group. These patients were further sub divided into Sub clinically hypothyroid(Sh) (n=48; TSH above 6.1 µIU/ml with normal T_4 and T_3 levels) and Overtly hypothyroid(Oh) (n=48) with TSH ≥ 6.0 µIU/ml and/ or abnormally low T4(below 4.8 µg/dl) and T3(below 0.6ng/ml) levels.

Descriptive Statistics and analysis of the data: Purposive sampling method was employed for the collection of the relevant data. The total no of patients who met the purpose of the study were 150**.**

The data about age, BMI and all the required biochemical parameters for each patient was collected on a well-designed data entry form.

The data so obtained was statistically analyzed using SPSS for windows 21.0 software and Microsoft Excel. Values were reported as mean ± standard error of mean. Pearson's correlation of the data was also carried out to look for association between variables. A, p value of < 0.05 was considered to be significant.

RESULTS

The total no of patients visiting various outpatient departments during the study period were 539968. Out of which 281,311 were female and 258,657 male. The total referral cases from these departments for thyroid screenings were 15667. The newly diagnosed cases of thyroidal dysfunctions were 3010.The female were 2303 and male were707. The ratio of female and male was 3.26:1. Out of total females patients 553 were below 18 years, 340 were pregnant, 952 female were sufferings from various other diseases like kidney, liver, bone, heart ailment, diabetes and hence were excluded from the study. Two hundred and eight were found non pregnant women having abnormal thyroid profile .One hundred and twelve were hyper thyroids patients and hence not included in the study. The 96 patients were hypothyroid and were selected for this study. The control group consisting of 54 non pregnant women was selected from the patient having normal thyroid profile. The characteristics of the patients and control groups are presented below.

Base line characteristic of the study group: The Study and Control groups were age matched 150 Non-Pregnant Women (NPW). The mean age of patients in the control group (N) was 42.15 ± 1.86 years, 46±18 years for Overtly hypothyroid (Oh) and 45.97±1.93 years for Sub clinically hypothyroid (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). The %age of M, EPM and LPM in the Oh(48) and Sh(48) group were, 54.16%(26), 12.5%(06), 33.83%(16) and 45.83%(22), 22.92%(11), 31.25%(15) respectively.

Comparison of the thyroid profile and renal markers of the study group: The serum values of thyroid profile and renal markers are given in table no1. The mean serum level of TSH was found to be lowest in N group (2.38± 0.49µIU/ ml) and highest in the Oh group (25.89±2.86µIU/ ml). Serum T_3 level was highest

in N group (1.68± .005ng/ml) and lowest in Oh group (0.94±0.09ng/ml). Highest serum T_4 level was found for N group (8.50±1.59µg/ dl) and lowest in Oh group (4.30±0.28µg/ dl).

Mean serum creatinine was highest in N group (1.47±1.25mg/dl) and lowest in Oh group (1.10±0.01mg/dl).Mean serum urea level was highest for N group (32.60±1.22mg/ dl) and lowest for Sh group (23.22±0.88 mg/dl).

Table No.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	48	25.89±2.86	0.94±0.09	4.30±028	1.10±0.01	30.11±1.25
3	Sh	48	19.04±2.22	1.47±0.08	7.07±0.38	1.18±0.04	23.22±0.88

N: Normal, Oh: Overtly hypothyroid, Sh: Sub clinically hypothyroid
TSH: Thyroid Stimulating Hormone, T_3: Triiodothyronine, T_4: Tetraiodothyronine

Table No. 2:Multiple linear regression analysis of thyroid profile withBMI and renal markers in the N,OhandSh group

Group ID		N			Oh			Sh		
Dependent variables		BMI	Cret	Urea	BMI	Cret	Urea	BMI	Cret	Urea
Constant		30.48	0.58	38.92	23.4	0.83	24.7	23.3	0.58	29.99
Independent variables	TSH	0.35	0.12	0.03	0.05	0.01	0.02	0.01	0.002	-0.04
	T_3	-0.12	-0.90	0.86	-0.40	0.03	-3.27	0.73	0.19	2.50
	T_4	-0.80	0.15	-0.92	-0.08	0.09	0.66	-0.18	0.01	-0.64

Regression analysis of the study group: Multiple linear regression analysis using thyroid profile markers(TSH,T_3 and T_4) as independent variables while BMI, Serum Cretinine and urea as dependent variable was carried out for all the three study groups and the results are presented in table -2.

Table No.3:Correlation analysis of renal markers with TSH, T_3 andT_4 in the various groups.

Parameter	Group ID	Renal biochemical markers	
		S.Cret	S. Urea
		r (p)	r (p)
TSH	N	0.19 (0.17)	0.01(0.98)
	Oh	0.06 (0.67)	0.02(0.90)
	Sh	-0.13 (0.40)	-0.01**(0.05)
T_3	N	-0.27* (0.05)	0.004(0.98)
	Oh	0.07 (0.65)	-0.21(0.15)
	Sh	0.40** (0.01)	0.16(0.22)
T_4	N	0.13(0.33)	-0.16(0.26)
	Oh	0.19 (0.19)	0.07(0.63)
	Sh	0.18 (0.21)	-0.12 (0.40)

*. p <0.05(significant)

BMI was found to be positively related with TSH and negatively related with T_4 in all the study groups. BMI showed positive relation with T_3 only in Sh group and negative in N and Oh group. Serum creatinine showed positive relation with TSH, T_3 and T_4 in all the study groups. It showed only negative relation with T_3 in the N group. Serum urea showed positive relation with TSH in N and Oh group, with T_3 in N and Sh group and with T_4 in the Oh group. Serum urea showed negative relation with TSH in Sh group, with T_3 in Oh group and with T_4 in N ad Sh group respectively.

Correlation analysis: The Pearson's correlations of renal markers and thyroid profile markers function were analyzed as shown table-3. Serum Creatinine showed a very significant positive correlation with T_3 in the Sh group (p= 0.005) and negatively correlated with T_3 in the N group (p= 0.05).Urea was significantly negatively correlated with TSH in Sh group (p= 0.05).

DISCUSSION

In the present Cross Sectional Hospital based study, we examined the serum Biochemical Markers (BM) of Renal Function (RF)in Normal (N) non-pregnant women and compared it with hypothyroid(Oh & Sh group) non- pregnant women.

In our study we found a minor decrease in the serum creatinin level in the Oh(1.10mg/dl) and Sh group(1.18 mg/dl) as compare to N group(1.47mg/ dl).The findings of this study are in good agreement with the notion that Serum Creatinine virtually remain unchanged due a balance created between the decrease in Renal Clearance (RC) and decrease generation[18].

Some studies have reported the elevation of serum creatinnie in the hypothyroid subjects but it includes all the sexes as against this study groups which includes only non- pregnant women [7]. More over the contradictions between the findings of various studies may be due to other factors like life style, food habits, medical history, geographical locations and genetical differences which were not taken into considerations.

Serum urea was found slightly decreased in the Sh group (23.22 mg/dl) as compared to N group (32.60mg/dl) and Oh group (30.11mg/dl). This minor decrease was insignificant and was in consistent with the other studies in which no significant effects were observed on serum urea levels in hypothyroid subject [19].Hyperuricemia in hypothyroid subjects has been reported in a few studies done around the world[20, 21]. A few studies report the effects of hypothyroidism on Serum Creatinine and Serum Urea levels, literature survey did not show any significant study showing such correlations. Some studies have reported negative correlation of creatinine with T_3 and T_4 and positive correlation with TSH[22]. In our study Serum creatinine was found to be significantly positively correlated with T_3 in the Sh group(p= 0.005) and showed a significant negative correlation with T_3 in the N group (p= 0.05).Urea was significantly negatively correlated with TSH in Sh group (p= 0.05).

According to our view it is the first kind of study reporting the association of thyroid dysfunctions and its effects on renal markers from this part of northern Pakistan. Despite our best efforts we could not found any such study reporting the association between thyroid gland and kidney axis. These findings of our study will encourage researchers from this area to focus on this area of interest for better results.

The study has got a number 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, β- trace protein and urinary albumin which are considered better renal markers were not measured due to lack of laboratory facilities and financial constraints. Lastly the study was carried out in one center, involving only 150 non- pregnant women and hence its findings cannot be generalized. Further studies are required involving larger populations for better results..

CONCLUSION

Hypothyroidism is a common problem in northern Pakistan affecting women folks more as compared to other gender due to lack of education and health facilities in rural areas. The other important conclusion which we assume to be most important is the lack of adequate amount of iodine in drinking water and iodized salt due to lack of strict quality control. We also conclude from our study that Hypothyroidism may not affect renal functions in non-pregnant women from this part of northern Pakistan.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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