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Research Article

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Correlation analysis of thyroid antibodies (anti-thyroid peroxidase AntiTPO and anti-thyroglobulin Anti TG) with thyroid stimulating hormone (TSH), Thyroid hormones (T3, T4) and disease status in selected population

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Abstract *Background:* Thyroid auto-immunity a disorder is now prevalent, consisting of poly-dimensional outcomes and mostly noted in females aged 30-50 yrs. Moreover generic thyroid dysfunction, sub-clinical or overt hyper and hypothyroidism are now a commonality in populous of both developed and underdeveloped countries. *Aim:* The present study assesses the correlation among antiTg and anti-TPO with thyroid hormones and thyroid stimulating hormone (TSH) in addition to relation with thyroid disease status. *Materials and Methods:* Anti TG, anti-TPO, thyroid hormones (T3 and T4) and TSH were determined in 200 selected individuals, including 112 females (56%) and 88 males (44%) using electro-chemi-luminescence technology on Cobas e411 (Roche, Diagnostics, Basil). *Results:* Both auto-antibodies correlated with each other generating R^2 of 0.9605. AntiTPO compatibility with TSH showed compatible linear-relationship of (y = 1.599x + 30.986) R2 = 0.8394, whereas anti-TG data vs TSH exhibiting a higher level of correlation (y = 0.7327x + 43.26) R2 = 0.9377. Comparative analysis of antiTPO with T3 also manifested good regression correlation of R2 0.7748 (y = 11.121x + 35.104) whereas antiTG vs T3 at a higher level (y = 4.9798x + 45.931) R^2 0.8246. *Conclusion:* Data presented here suggested exploratory significance of anti-thyroid antibodies in relation to the existence of elevated levels of TSH and thyroid hormones in patients with generic as well as autoimmune thyroid disorders.

Keywords Anti-Tg (anti-thyroglobulin antibodies), AntiTPO (anti-thyroid peroxidase), electro-chemi-luminescence (ECL) technology

Introduction

In last few decades, one of the central diagnostic parameter, anti-thyroid auto-antibodies, consisting of anti-Tg (anti-thyroglobulin antibodies) and antiTPO (anti-thyroid peroxidase) were introduced to assess the autoimmunity of thyroid disorders [1-3]. Currently both anti-TG and antiTPO are used in combination of thyroid hormones to evaluate thyroid status of suspected individuals and to manage the treatment regiments [3,4].

Thyroid dysfunction per se, including sub-clinical or overt hyper and hypothyroidism and autoimmune thyroid disease are now a commonality in both developed and underdeveloped countries [3, 5-8]. Moreover, overt endocrine dysfunctions are now more frequent affecting 5-10% of suspected patients [9]. In this regard thyroid auto-immunity (TAA) disorders and production of auto-antibodies is getting considerable attention by clinicians and scientist due to its poly-dimensional outcomes. Furthermore, clinical data also support its significance due the fact that, TAA mostly

affect females aged 30-50 yrs [3, 10]. Nonetheless, it was reported that prevalence rate of TAA progressed with patients' aging, in which 2-4% women and 1% of men are suspected to have full clinical symptoms [11].
The present study was undertaken to evaluate correlation of antiTg and anti-TPO with thyroid hormones and thyroid stimulating hormone (TSH) in addition to relation with thyroid disease status.

Materials and Methods

Study Design and patients

anti TG, anti-TPO, thyroid hormones (T3, T4) and TSH were determined in 200 selected individuals, including 112 females (56%) and 88 males (44%). The study period was Dec 2015 to Dec 2017 at Department of Biochemistry Lab services and Chemical Pathology, Liaquat National Hospital and Medical College. Average age of females was 45.20 ± 8.10 yrs and that of males 50.45 ± 7.50 yrs. All of the individuals were either confirmed cases of thyroid disorders, or under-treatment, recently diagnosed cases, as well as those with overt/sub-clinical thyroid anomalies. Age, gender, occupation, locality, any other disease forms, pregnancy data were collected and correlated with the assessments, where applicable. Care was taken that none of the patients had any history of operations, malignancies, liver or renal disease, interferon therapies or β-blockers usage.

Blood collection

Six milliliters whole blood was collected from each patient and 40 healthy individual in Clot-activated tubes (Red Top). Serum was separated and stored at -20^{o}C. Where needed, dilution and aliquots were prepared to get actual quantitation of all parameters.

Analytical determinations

Anti-Tg, Anti-TPO antibodies, tri-iodothyronine (T3), tetra-iodothyronine (T4) and TSH were measured using electro-chemi-luminescence technology on Cobas e411 (Roche Diagnostics, Basil) with normal references ranges of <115 IU/ml, < 34 IU/ml, 0.8-2.00 ng/ml, 5.1-14.1 μg/ml, 0.27-4.2 μlU/ml, respectively. AntiTg and TSH analysis was performed by two step sandwich ECL immunoassay, whereas antiTPO, T3, T4 and TSH by competitive ECL immunoassay.

Statistical analysis

All data was statistically analyzed by SPSS ver 17 (USA) through Student's t-test, paired and by using regression correlation analysis R^2 among thyroid hormones and thyroid antibodies. Data considered to be significant when $P < 0.05$ and presented as Mean ± SD.

Results

A total of 200 patients were selected for present study, of which 112 were females and 88 males. This selected group was screened through 354 patients over a period of one year (Jan 2015 till Dec 2017) to ensure that only those who fall within our criteria of abnormal thyroid functions were considered and assessed. All individual that were selected were suffering from confirmed thyroid disorders, most of which exhibited markedly elevated anti-thyroid antibodies. Regression correlation analysis showed strong linearity of compared parameters. Both auto-antibodies correlated with each other generating R^2 of 0.9605, which means 96.05% data compatibility among both parameters and linearity in results as well ($y = 1.8767x - 43.347$) $R^2 = 0.9605$ (Fig 1). When antiTPO was compared with TSH, R^2 correlation data came out with compatible linear-relationship of R^2 0.8394 ($y = 1.599x + 30.986$), depicting that thyroid antibodies correlated well with TSH concentration changes (Fig 2). However, anti-TG data comparison with TSH exhibited a much higher level of correlation ($y = 0.7327x + 43.26$) $R^2 = 0.9377$ (Fig 3). Comparative analysis of antiTPO with T3 also manifested good regression correlation of ($y = 11.121x + 35.104$) $R^2 = 0.7748$ (Fig 4) whereas antiTG vs T3 at a higher level ($y = 4.9798x + 45.931$) $R^2 = 0.8246$ (Fig 5). T4 comparative grouping with antiTPO and antiTg showed comparatively lower but good levels of regression correlation with antiTPO vs T4 = ($y = 1.1649x + 60.311$) $R^2 = 0.7386$ (Fig 6) and that of antiTg vs T4 = R^2 0.7151 ($y = 0.4975x + 58.234$) (Fig 7). In summary the strongest regression correlation of > 80% was noted in the group compared, antiTg vs TSH and antiTPO vs TSH, whereas good correlation with T3 and T4 at the level of > 70%.

Fig 1: Comparative analysis of Anti TPO vs Anti TG

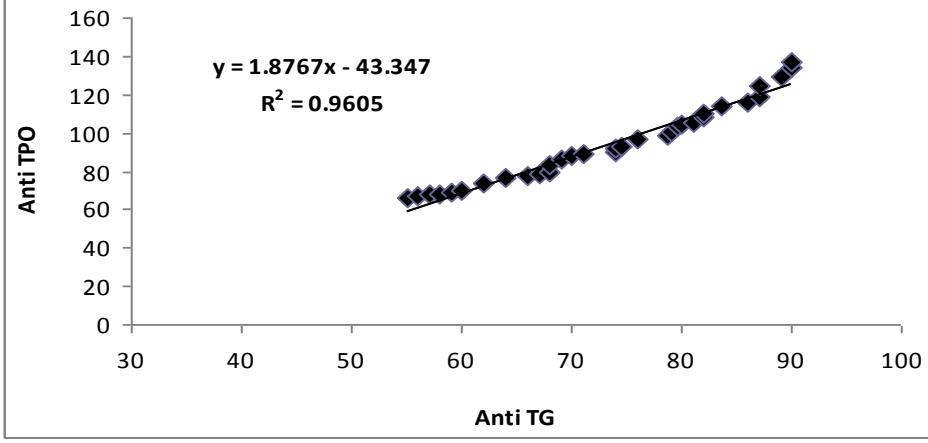


Fig 2: Compapartive analysis of Anti TPO vs TSH

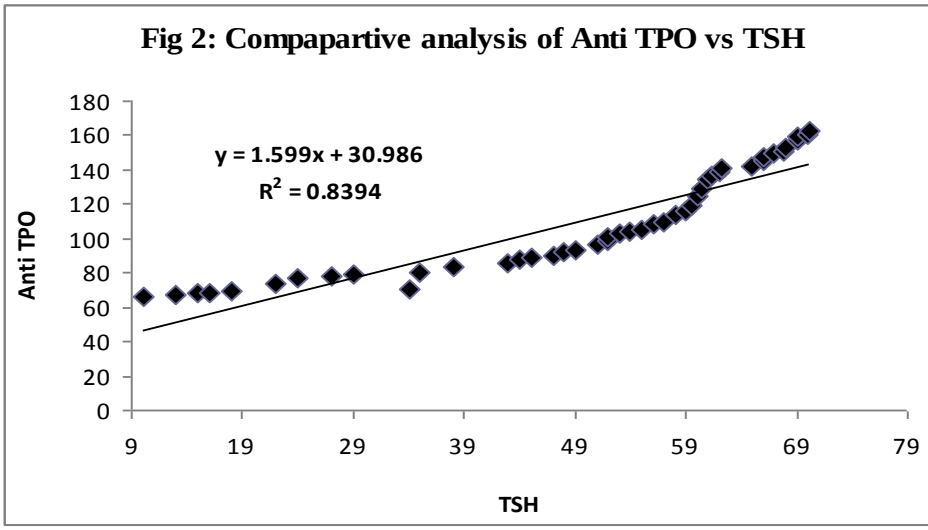
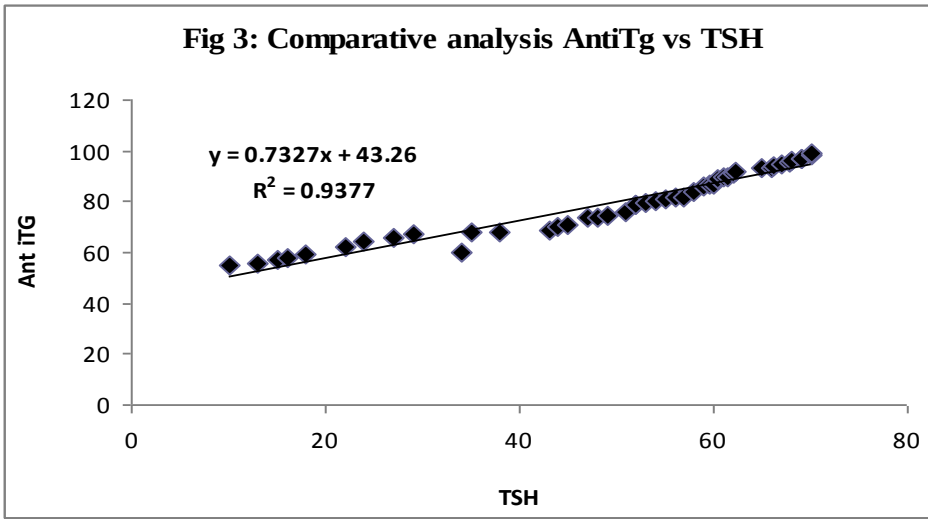


Fig 3: Comparative analysis AntiTg vs TSH



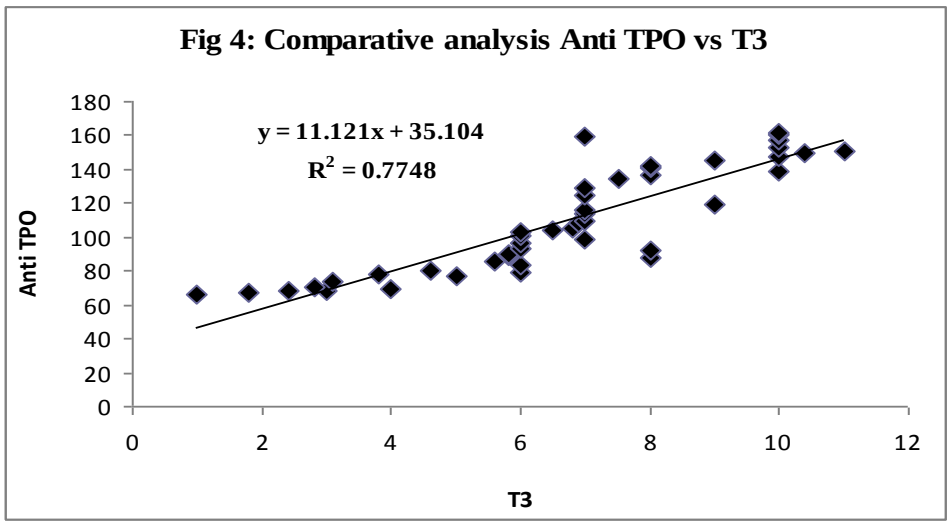


Fig 4: Comparative analysis Anti TPO vs T3
y = 11.121x + 35.104
R2 = 0.7748
Anti TPO
T3
0
20
40
60
80
100
120
140
160
180
0
2
4
6
8
10
12

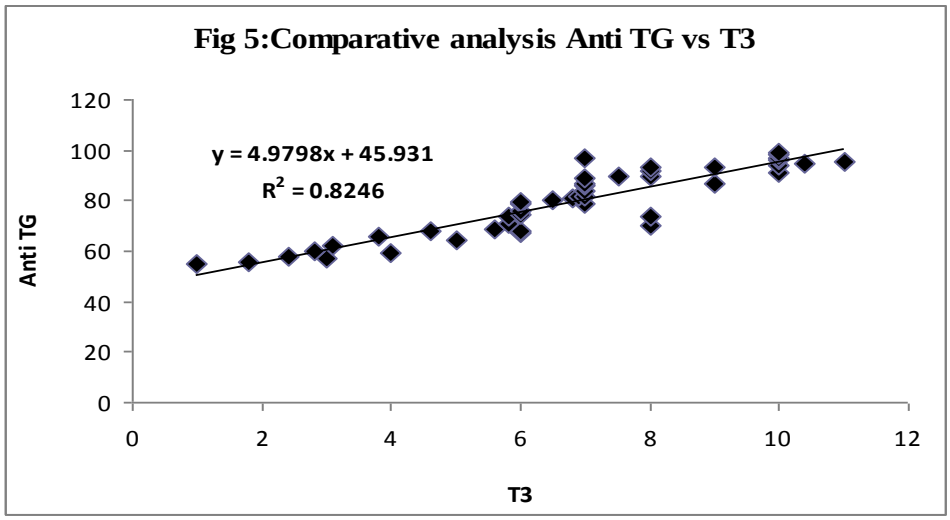


Fig 5:Comparative analysis Anti TG vs T3
y = 4.9798x + 45.931
R2 = 0.8246
Anti TG
T3
0
20
40
60
80
100
120
0
2
4
6
8
10
12

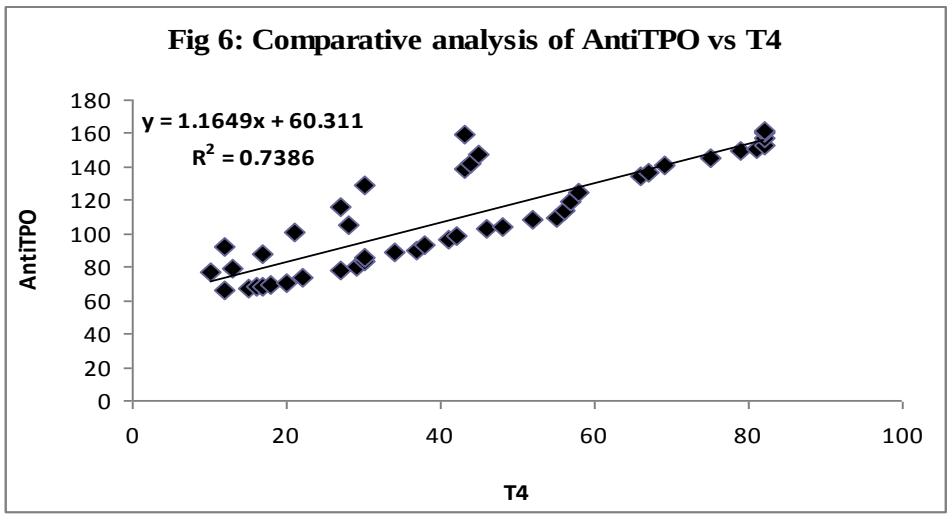
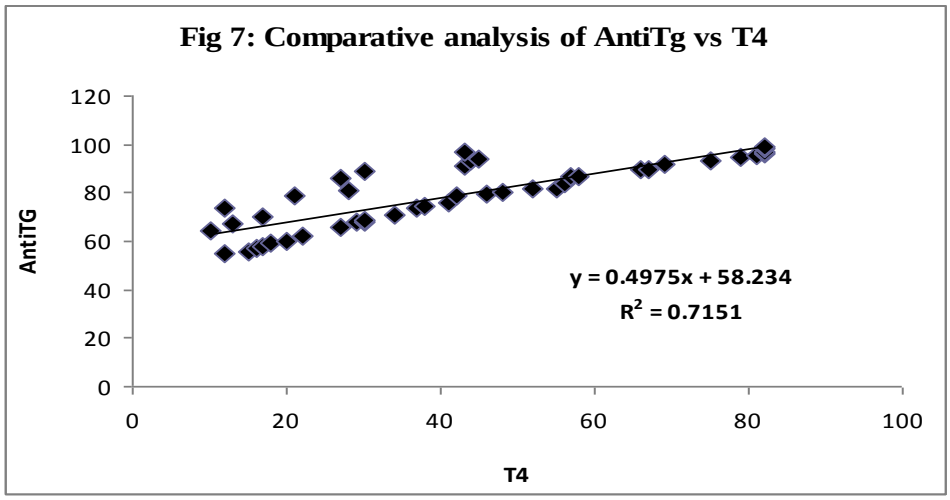


Fig 6: Comparative analysis of AntiTPO vs T4
y = 1.1649x + 60.311
R2 = 0.7386
AntiTPO
T4
0
20
40
60
80
100
120
140
160
180
0
20
40
60
80
100



Discussion

It was well reported in scientific and clinical literature that one of the autoantibodies, antiTPO, is an important diagnostic tool regarding autoimmune thyroid disorders, generic thyroid disease, overt conditions and assessment of treatment progression and outcomes [3, 12-14]. However, 10% normal population also exhibited antiTPO, in addition to its presence in 30% elderly individuals [14]. Several recent and past reports also mentioned presence of antiTPO in sub-clinical hypothyroidism [7, 9], therefore causing suspicions of developing overt hypothyroidism in the later stage of the life [9]. Therefore, carefully crafted and centered studies pointed out greater clinical significance of antiTPO and anti-TG as probable indicator of pathogentic background [3]. Furthermore several studies also noted antiTPO proportional correlations with autoimmune based thyroiditis [15], in addition to having high anti-Tg level as well [16].

The present study in this regard was undertaken to assess correlation among thyroid antibodies viz antiTg and AntiTPO, thyroid hormones viz T3 and T4 and thyroid stimulating hormone, TSH, and noted linear regression ranging from significantly high to good. It was noted that very strong correlation existed among antiTG vs TSH and antiTg vs T3 followed by antiTPO vs TSH. Moderate correlation was exhibited when antiTPO and antiTg were compared with T4.

As observed in our study, positive regression correlation of antiTPO was reported in a previous study where around 64.45% of the patients have tested for TSH with elevated levels and exhibited markedly high antiTPO concentrations [3]. Conclusion was drawn that those patients with high TSH should have got their anti TPO necessarily tested for the diagnosis of autoimmune hypothyroidism.

Regarding anti-TG, it was reported that only 15.4% selected population showed correlation [7], however another study [4] reported a positive correlation (R = 0.51) of TSH with anti-TG. This data is in similarity to our findings, where antiTg is proportionally correlated with TSH and with T3, T4 as well. Some previous work also emphasize in establishing community-based reference for fT4 and TSH in relation to prevalence of anti-Tg and anti-TPO [17]. Nonetheless it was suggested that those patients showing elevated concentration of both antibodies, consequently suffering from auto-immune disorders [18]. It was also noted in a study that antiTg and antiTPO positive/linear correlation existed more strongly in females than males [7] and strongly in females over the age of 50 yrs.

In conclusion, the present study describes the assessment and correlation of antiTg and anti-TPO with thyroid hormones, T3 and T4 and thyroid stimulating hormone (TSH) in addition to relation with thyroid disease status in 112 female and 88 male patients. It was noted that both antibodies correlated well with each with R^2 of 0.9605, whereas individually, antiTG correlated well with TSH (R^2 0.9377) and T3 (R^2 0.8246) and anti-TPO considerably with TSH (R^2 0.8394). All patients were noted to be suffering from confirmed cases of thyroid disorders (mainly hypothyroidism, followed by hyperthyroidism), or under-treatment, recently diagnosed cases, as well as those with

overt/sub-clinical thyroid anomalies. Data suggested investigative significance of anti-thyroid antibodies in relation to the existence of elevated levels of TSH and thyroid hormones.

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