International Journal of Research and Review
www.ijrrjournal.com E-ISSN: 2349-9788; P-ISSN: 2454-2237

Original Research Article

Association of Serum TNF-Alpha with Thyroid Parameters: A Hospital Based Study

Dr Piali Choudhury[1], Dr. Sandip Chakraborty[2], Dr Aihik Saha[3], Sayan Mazumder[4]

[1]Demonstrator, [2]Associate Professor, [3]Postgraduate Trainee,
Department of Biochemistry, Nil Ratan Sircar Medical College, Kolkata, West Bengal
[4]M.Sc Biochemistry Student, Oriental Institute of Science and technology, West Bengal

Corresponding Author: Dr. Sandip Chakraborty

ABSTRACT

Auto-immune thyroiditis is one of the leading causes of thyroid dysfunction. However, the clinical presentation of the autoimmune thyroiditis shows a wide array of clinical presentation. The patients may remain clinically silent or even present with overt hypothyroidism. Studies suggest that autoimmune thyroiditis may result due to interplay of cytokines like C-reactive protein, interleukin-6 and tumor necrosis factor-alpha (TNF-α). Recent studies have seen an extensive role of inflammatory marker TNF-α in the regulation of thyroid transcription factor. This study was done to estimate the serum concentration of TNF-α in patients suffering from thyroid disorder and to see its variation from healthy controls. In this cross-sectional study serum TSH, Free T4 and TNF-α concentration was estimated in patients of thyroid dysfunction patients and compared with control group. Statistical analysis was performed using SPSS 21 and serum concentration of TNF-α was significantly higher in cases ($p<0.05$).

Key words: TNF-α, thyroid dysfunction, Auto-immune thyroiditis

INTRODUCTION

Primary hypothyroidism is one of the most common endocrine disorder and results mostly due autoimmune thyroiditis. [1] Hashimoto's thyroiditis and Grave's disease are the two-types of autoimmune thyroid disorder. These diseases have a wide array of clinical presentation, from silent to overt hypothyroidism. Studies suggest that hypothyroidism is an inflammatory condition due to cytokines like cytokines like C-reactive protein, interleukin-6 and tumor necrosis factor –alpha (TNF-α). [2] These cytokines leads to many hypothyroidism associated complications like endothelial dysfunction, proliferation of smooth muscles, and recruitment of inflammatory cells. [3] TNF-α, produced by macrophages, monocytes, lymphocytes and induces production of interferon γ and leads to apoptosis. [4,5] Reports indicate that TNF-α are produced in chronic thyroiditis, subacute thyroiditis and lead to destruction of thyroid follicular cells. [6] Moreover, TNF-α leads to modulation of thyroid function and administration of TNF-α in animal models may lead to raised TSH concentrations and reduce iodine uptake. [7] In support to this, there is evidence of thyroid dysfunction of patients taking Etanercept in patients of Psoriasis Vulgaris. [8] This study has been done to find whether TNF-α has a role in diagnosing and classifying patients has hypothyroid due to auto-immune hypothyroidism.

MATERIALS AND METHODS

This study is a hospital based cross sectional study a based on the measurement of TNF-α in serum of newly diagnosed hypothyroid patients and healthy controls. For this purpose, blood samples were drawn from 35 hypothyroid patients diagnosed by history, physical examinations & routine laboratory investigation. The study was conducted after receiving approval from the ethical committee of NRS Medical College. The samples were collected after obtaining consent from both patients and control. Patients free from any thyroid disease, and infection were selected as control (Age & gender matched). Patients with previously history of thyroid disease, drug history of iodine containing drugs, radioactive iodine, other endocrine dysfunction, acute infection and smoking were excluded. The estimation of TSH, free T4 and TNF-α was done in the O.P.D Clinical Biochemistry Laboratory of Nil RatanSircar Medical College and Hospital, Kolkata within the study period of one month. Serum TSH, free T4 and TNF-α was estimated using ELISA.

Statistical methods:

The values of TSH, free T4 and TNF-α the cases as well as healthy controls were extrapolated in Microsoft excel. The data was analysed using IBM SPSS software version 21. The data was checked for normal distribution using Kolmogorov - Smirnov test and Shapiro-. The values were normally distributed as P > 0.05.The mean values were estimated and compared using Student's T-test. However, the TNF-α was not in Gaussian distribution and thus they were compared using Mann-Whitney's test. The p values less than 0.05 were considered statistically significant.

RESULTS

The mean concentration of TSH in the diseased patient was significantly higher than the controls. ($p<0.05$), as evident from Table1.However,the mean values of serum free T4 was higher in healthy controls in comparison to diseased patients as evident from table 1. However, there was no significant difference ($p>0.05$).

Table: 1 Showing the mean values of TSH and free T4,expressed Mean+ SEM

SL.NO	GROUP	Mean TSH(μIU/ml)	Mean fT4 (ng/dl)	Independent t-Test
1.	Hypothyroid Patients	6.96+0.99	0.84+0.16	p=0.000
2.	Healthy Control	1.99+ 0.617	1.12+ 0.22	p=0.05

* P<0.5 considered as statistically significant

Table: 2 Showing the median values of TNF-α expressed as median +Interquartile range.

sl.no	Group	Median+ IQR (pg/ml)
1.	Hypothyroid Patients	407+150.78
2.	Healthy control	57+17.53

At the significance level of 0.05, the asymptotic significance of Mann-Whitney's was 0.000 ($P<0.05$). That shows the difference between two values were statistically significant

DISCUSSION

After statistical analysis it is evident, that the mean concentration of TNF-α is significantly in hypothyroid patients. Moreover, the findings of our studies are in accordance with study of Li &Zhou et al. [9] suggesting that the levels of TNF-α in patients with Grave's disease. Moreover, literature review suggested the hypothyroidism may be associated with histocompatibility leucocyte antigens and closely linked immunomodulatory genes. [10] Both subclinical and overt hypothyroidism states have been found to be associated with auto-immune thyroiditis. The study findings are also in accordance with the findings of Inoue and et al though in animal model. [7] It has been postulated that TNF-α production may be associated with production of Thyroid receptor antibody (IgG1) that is active in Graves disease. [11] The pathophysiology may be TNF-α promotes the production of antibody IgG1 class. However, the study requires simultaneous assessment of TRAb too. However these are costly parameters. Despite the constraints of limited sample

size it is well established that TNF-α is increased in hypothyroid patients.

CONCLUSION

Despite the constraints of small sample size, increased concentration of TNF-α is involved in the aetiopathogenesis of autoimmune thyroid destruction. However, the role of TNF-α in inflammatory process of auto-immune thyroiditis needs correlation with anti-TPO antibody and requires study with more subjects. Moreover, analysis of other parameters like thyroid hormone receptor antibody, thyroglobulin may strengthen the study results and elucidate the role of TNF-α as a routine marker of thyroid dysfunction.

ACKNOWLEDGEMENTS

The authors of this article acknowledge gratitude the researchers whose studies have been referred. All those who have significantly contributed in this study are included as author. All the authors are grateful to all the study participants who have given their blood for analysis and actively participated in the study.

REFERENCES

1. Larry Jameson J, Anthony Weetman A. Disorders of thyroid gland. Harrison's Principles of Internal Medicine. 18th ed. USA: McGraw Hill Publishers; 2012. p. 29182.Wilson AM, Ryan MC, Boyle AJ (2006).
2. Cleare AJ, McGregor A, O'Keane V. Neuroendocrine evidence for an association between hypothyroidism, reduced central 5-HT activity and depression. Clin Endocrinol (Oxf) 1995;43:713-9.
3. Schuett H, Luchtefeld M, Grothusen C, Grote K, Schieffer B. How much is too much? Interleukin-6 and its signalling in atherosclerosis. Thromb Haemost 2009; 102:215-22.
4. Matsuno H, Yudoh K, Katayama Ret al. The role of TNF-alpha in the pathogenesis of inflammation and joint destruction in rheumatoid arthritis (RA): a study using a human RA/SCID mousechimera. Rheumatology (Oxford) 2002;41:329–37.
5. Scheurich P, Thoma B, Ucer U, Pfizenmaier K. Immunoregulatoryactivity of recombinant human tumor necrosis factor (TNF)-alpha: induction of TNF receptors on human T cells and TNF-alpha-mediated enhancement of T cell responses. J Immunol 1987;138:1786–90.
6. Volpe R1988 Subacute thyroiditis. In: Ingbar SH, Braverman LE (eds) TheThyroid, ed 5. Lippincott, Philadelphia, pp 1106 –1119.
7. Masayuki Ohmori, Norikazu Harii, Toyoshi Endo, Toshimasa Onaya, Tumor Necrosis Factor-α Regulation of Thyroid Transcription Factor-1 and Pax-8 in Rat Thyroid FRTL-5 Cells, *Endocrinology*, Volume 140, Issue 10, 1 October 1999, Pages 4651–4658, https://doi.org/10.1210/endo.140.10.7021.
8. Ioana Roman, Iulia & Mocan, Teodora & Orasan, Meda & Mihaela Jianu, Elena & Sfrangeu, Carmen-Angela & Orasan, Remus-Ioan. (2017). Relationship between etanercept and thyroid function in patients with psoriasis vulgaris. Clujul Medical. 91. 10.15386/cjmed-813.
9. Li N, Zhou Z, Liu Xet al.Association of tumour necrosis factoralpha (TNF-alpha) polymorphisms with Graves' disease: a meta-analysis. Clin Biochem 2008;41:881–6.
10. Hunt PJ, Marshall SE, Weetman AP et al. Histocompatibility leucocyte antigens and closely linked immunomodulatory genes in autoimmune thyroid disease. Clin Endocrinol (Oxf) 2001;55:491–9.
11. Weetman AP, Yateman ME, Ealey PA et al. Thyroid-stimulating antibody activity between different immunoglobulin G subclasses. J Clin Invest 1990;86:723–7.

How to cite this article: Choudhury P, Chakraborty S, Saha A et.al. Association of serum TNF-Alpha with thyroid parameters: a hospital based study. International Journal of Research and Review. 2019; 6(6):30-32.

******