How to Cite:
Shahrukh, M., Masood, T., & Saxena, S. (2022). Correlation of tumor necrosis factor alpha (TNF-α) with thyroid hormones (TSH, Free T3 & Free T4) in the patients of subclinical hypothyroidism. *International Journal of Health Sciences*, *6*(S5), 12211–12217. https://doi.org/10.53730/ijhs.v6nS5.11967

Correlation of tumor necrosis factor alpha (TNF-α) with thyroid hormones (TSH, Free T3 & Free T4) in the patients of subclinical hypothyroidism

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***Abstract*---**Background: Subclinical hypothyroidism is a minor form of hypothyroidism caused by a high TSH level. TNF-α one of the suggested parameters to detect thyroid disorders, it is involved in various purposes such as inflammatory skin disease, cardiovascular function, endothelial dysfunction etc. Objective: The goal of this research was to determine the relationship between Tumor necrosis factors-α and thyroid profile in subclinical hypothyroidism, including its predictive value. Method: The current study included 200 patients and 200 controls who consulted the outpatient departments of Shri Guru Ram Rai Institute of Medical and Health Sciences in Dehradun and Rohilkhand Medical College Hospital in Bareilly. These participants' biochemical parameters (TSH, FT3, FT4, & TNF-) were investigated using the ELISA method. Result: TNF-α level was found to be comparatively greater in cases (mean ± SD value- 38.66 ±37.59) of subclinical hypothyroidism as compared to controls (mean ± SD value-3.47±3.29) in the study. Conclusion: The current investigation found that TNF- played a significant role. TNF- α effective marker to find out the thyroid disorder but TSH is far more effective than TNF-α to detect thyroid abnormalities.

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 9 April 2022, Manuscript revised: 18 June 2022, Accepted for publication: 27 July 2022

***Keywords*---**sub-clinical hypothyroidism, TSH, FT3, FT4, TNF-α.

Introduction

The patient who has normal free T4 and free T3 level but a little increased serum TSH level is the one who was initially referred to as having subclinical hypothyroidism. Preclinical hypothyroidism, reduced thyroid reserve, and mild hypothyroidism are other names for this syndrome. With values often falling between 4 to 15 mU/L, the TSH rise in these patients is mild, while those with values above 10 mU/L are more likely to have decreased free T4 and might exhibit some hypothyroid symptoms. The reference range for a normal TSH concentration has a considerable impact on the classification of this illness (*Harrison's Principles of Internal Medicine, 20th Edition 1*, n.d.). Most of the subclinical hypothyroid Patients have nonspecific symptoms and identified during routine blood tests. The prevalence of subclinical hypothyroidism has been observed to be 6% to 14% in different geographical areas [(Gupta et al., 2015). This syndrome, which affects 7% to 10% of older women, is most frequently observed in people with early Hashimoto's disease. The common etiology of this illness is hypothyroidism, which is not well treated, and autoimmune gland disease (Cooper, 2001).

TNF-α is a cytokine with multiple immunological and metabolic functions. Prior research suggested that TNF- was also produced by smooth muscle cells, cardiac myocytes, endothelium and epithelial cells, and activated macrophages and lymphocytes of the immune system. Recent studies have shown that TNF- is a crucial pro-inflammatory cytokine and a crucial component of the innate immune system, which, when pattern recognition receptors are stimulated, stimulates the production of genes needed to regulate tissue inflammation and injury (Gupta et al., 2015, Mishra et al., 2018).

Aims and Objectives

Aim: Correlation of TNF-α with Thyroid Hormones (Free T3, Free T4 and TSH) in the patients of Subclinical Hypothyroidism.

Objectives:

- To estimate thyroid hormones (Free T3, Free T4 and TSH)
- To estimate Tumor necrosis factor alpha (TNF-α)
- Comparison and Correlation of thyroid hormones with TNF-α

Material and Methods

Samples were collected from patients who attended the outpatient department (OPD) at the Shri Guru Ram Rai Institute of Medical and Health Sciences in Dehradun and Rohilkhand Medical College and Hospital in Bareilly for a year between February 2021 and March 2022. Based on a simple random sampling technique that fulfilled the sampling selection requirements, subjects attended. The individuals' ages between >18 and 70 were recorded, along with their gender. Overt hypothyroidism, patients taking any anti-thyroid medication, patients

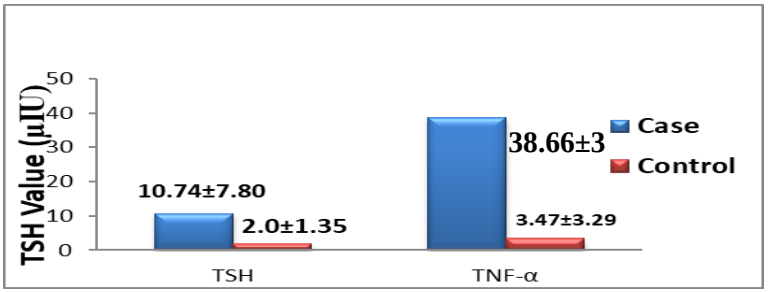
recovering from thyroid surgery, patients taking iodine- or iodide-containing medications, patients with a history of external radiotherapy of the neck, patients taking any anti-lipidemic medications, pregnant women, and people using oral contraceptives were all excluded. The TSH, FT3, FT4, and TNF- levels of all 400 patients (200 cases and 200 controls) were assessed. By using conventional techniques, the ELISA reader estimated each parameter.

Statistical Analysis

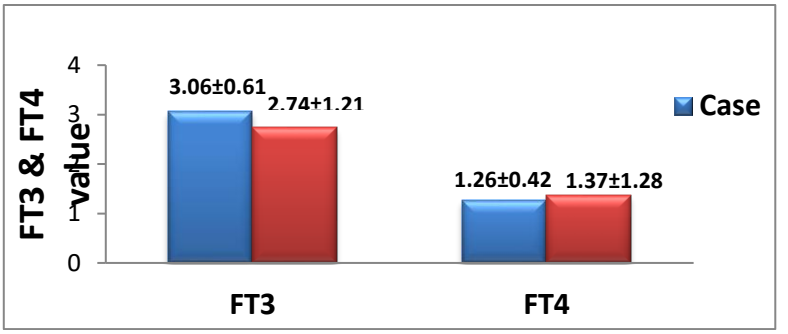
The statistical software for social sciences was used for the statistical analysis (SPSS). As necessary, several statistical techniques were applied. For quantitative data and frequency for categorical variables, mean SD was calculated. On all continuous variables, the independent t-test was run. Prior to any t-test, the data were verified for normal distribution. At p <0.05, differences were deemed significant.

Results

400 subjects (cases and controls) were involved in the current study. Out of 400 participants, 200 had subclinical hypothyroidism and 200 had normal thyroid function. These patients' TNF- and thyroid profiles were examined. The average age of the patients is 34.63±13.56 (Mean ± SD) years and the control group's average age is 36.67±14.55 (Mean ± SD) years. The no of male case is 62 (31%) and female case is 138 (69 %) out of 200 case subjects and the no male control is 63 (31.5 %) and female control is 137 (68.5%) out of 200 normal subjects. Graph chart 1 and 2 showing the Comparison of thyroid hormones and TNF-α between cases and control group (** <0.01highly significant, * <0.05significant).

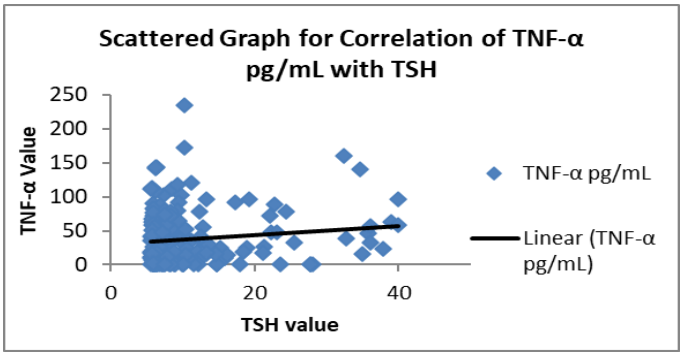


Graph Chart-1: Comparison of TSH and TNF-α between Cases and Control

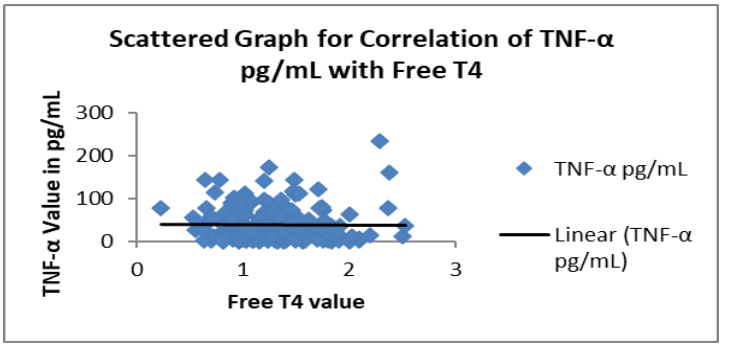


Graph Chart -2: Comparison of Free T3 & Free T4 between Cases and Control

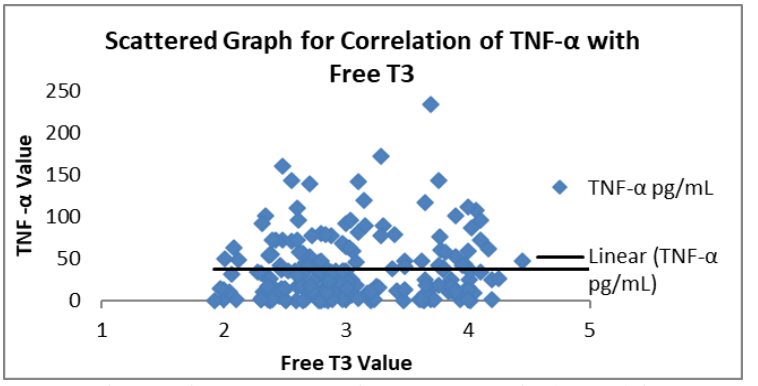
Comparing the thyroid profile and TNF- between the patients and the control group is shown in graph chart. TNF- mean and standard deviation value (38.66±37.59U/ml) is substantially higher in cases than control group (3.47±3.29 U/ml), Free T3 mean and standard deviation value (3.06±0.61pg/mL) and Free T4 (1.26±0.42ng/dL) is normal in both individuals, and TSH mean value (10.74±7.80IU/ml) is significantly higher in cases than control group (2.00±1.35IU/ml).



Scattered Graph-1: TSH has positive correlation with TNF-α.



Scattered Graph-2: Free T4 has no correlation with TNF-α



Scattered Graph-3: Free T3 has no correlation with TNF-α.

The scattered graphs 1-3 demonstrate the individual relationships between thyroid function and TNF-α. TNF- has a positive connection with TSH but no link

with Free T4 or Free T3.

Discussion

In this study we were observed higher level of TSH and TNF-α with normal level of Free T3 and Free T4. TSH mean value (10.58±7.66) is higher; TNF-α mean value (38.66±37.59) is also raised in study group than normal subjects. Free thyroxine (FT4) mean value (1.35±0.41) and tri-iodothyronine mean value (2.99±0.51) is normal in both subjects. According to Roseane C. et al., patients with subclinical hypothyroidism or those receiving pre-treatment for it had higher TNF- levels (122.8 U/ML). J. J. Dez et al. was demonstrated the connection of TNF-α system activation in subclinical hypothyroidism with high serum TNF-alpha concentration (3·17 ± 1·18 pg/ml) (Marchiori et al., 2015, Díez et al., 2002),

According to research by Parimal S. Tayde et al., depression and a poor quality of life are associated with the inflammatory state of primary autoimmune hypothyroidism, which is marked by an elevated level of inflammatory cytokines (TNF- alpha**)** (Tayde et al., 2017)**.** According to Savas Guzel et al.**,** increased levels of visfatin, leptin, and TNF- in overt and subclinical hypothyroid patients and the connections between these adipokines indicate their crucial involvement in the IR-associated diseases (Guzel et al., 2013).

According to Gluvic et al., thyroid hormones (TH) significantly affect cellular oxidative metabolism. Additionally, they promote the health of vascular smooth muscle and endothelial cells, maintaining vascular homeostasis. Target organs are affected by subclinical (SCH) and clinical (CH) hypothyroidism by changes in their morphology and function as well as by reduced blood and oxygen delivery brought on by accelerated atherosclerosis. One of the elements that contribute to inflammation is an elevated level of serum tumour necrosis factor alpha (Gluvic et al., 2022).

Guzin Fidan Yaylali et al. also noted elevated TNF alpha levels 49.06±9.96 (mean and standard deviation value) with p value 0.001 (highly significant <0.05) in Turkish patients with Hashimoto's thyroiditis and subclinical hypothyroidism. Additionally, he stated that TNF alpha and other inflammatory cytokines are crucial in the development of auto immune diseases and subclinical hypothyroidism(Fidan Yaylali, 2015). Olena Kolesnikov et al. described elevated TNF alpha (11.93 ±0.92) with p value 0.002 in non-alcoholic subclinical hypothyroidism patients, indicating the contribution of thyroid malfunction**.** During his study, he found that women under 50 who did not drink alcohol and had subclinical hypothyroidism had metabolic changes, the signs of which are affected by TSH levels of 10 mIU/mL or more (Kolesnikova et al., 2021**,** Sharma R et al., 2011)**,** Sarzosa Terán & Astudillo Calle, 2012)**.**

Esat Erdem Türemen et al. found that people with subclinical hypothyroidism had a higher level of TNF alpha p-value 0.002. he talked about Recently, one of the most talked-about topics has been the link between subclinical hypothyroidism (SH) and heart disease. There is still some disagreement about how it affects the heart and how to treat it. Age, body mass index, and waist circumference did not differ in a way that was important. There was a statistically

significant difference between the endothelium-dependent (FMD) and endothelium-independent (NTG) vascular responses of the patients with subclinical hypothyroidism and the normal healthy controls. In the patient group, the levels of TSH, LDL, IL-6, and TNF-alpha were all much higher than in the control group. Only endothelium-dependent vasodilation and TNF-alpha were found to have a positive relationship with each other (Esat Erdem Türemen1, 2011).

Conclusion

Out of all the investigations and observations only TSH is the better prognostic marker to ensure that the patients have subclinical hypothyroidism. In cases of mildly elevated TSH and TNF-α level is also a helpful prognostic inflammatory factor for subclinical hypothyroidism.

Acknowledgement

I would like to express my heartfelt gratitude to Dr. Tariq Masood, Professor and Head of the Biochemistry Department at the SGRR Institute of Medical and Health Sciences in Dehradun, and Dr. Shikha Saxena, Professor and Head of the Biochemistry Department of RMCH Medical College and Hospital Bareilly, for their advice and permission to conduct this work. I want to thank Dr. Arun Dean Research of SGRR University Dehradun from the bottom of my heart. I also want to thank my friends, coworkers, and family for all of their support and advice throughout the course of my whole study time. Last but not least, I would want to express my deepest appreciation to all of the patients who gave so much of themselves to this research and without whom it would not have been possible.

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