

Prevalence of Anti Thyroid Peroxidase Antibody in Hypothyroid Patient

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ABSTRACT

Background: Anti- Thyroid peroxidase (TPO) autoantibodies are very important in diagnosis of autoimmune thyroid diseases. It can be used as predictor of its clinical course from subclinical to overt hypothyroidism. Thus this study was conducted to describe the clinical manifestations of chronic Hashimoto's thyroiditis and prevalence of Anti TPO Antibodies in a population suffering from primary hypothyroidism. **Methodology:** The study was a hospital based, cross sectional study involving 50 cases, who presented with primary hypothyroidism to endocrine and medicine outpatient department between August 2015 to August 2016. The patients' history, physical examination, routine blood investigations and anti TPO Ab testing was done. Statistical analysis was done using SPSS 16 software. **Results:** Among 50 cases of primary hypothyroidism, 14 (28%) had TPO antibody positive. Female patients were more likely to be TPO antibody positive (37% vs 6.67% : F vs M). TPO positive patients had high mean TSH value (26.61 vs 13.39) as compared to that of TPO negative patients which was statistically significant ($p < 0.05$). The most frequent symptoms of TPO positive patients were lethargy, tingling sensation and weight gain and the most frequent signs were facial puffiness neck swelling and non-pitting pedal edema. **Conclusions:** Hashimoto's thyroiditis was the common cause of primary hypothyroidism in the study. It could not be differentiated on the basis of clinical presentation. Anti TPO Antibodies testing should be done in subclinical hypothyroidism.

Key words: Autoimmune, Anti Thyroid peroxidase, Hashimoto's thyroiditis, Hypothyroidism.

1. INTRODUCTION

Hypothyroidism is defined as a deficiency of thyroid activity, which results from reduced secretion of both T3 and T4 irrespective of the cause.¹ Anti-TPO autoantibodies are very important to diagnose autoimmune thyroid diseases and estimating its clinical course. Hashimoto's and Grave's are the commonly seen autoimmune thyroid diseases.² Antibodies to TPO are detectable in 50% to 90% of patients with Grave's disease. High antibody titers are found in 90% of patients with chronic Hashimoto's thyroiditis. Both thyroglobulin antibody and TPO antibody are found in almost 100% of such patients, but TPO Ab is of higher affinity and in higher concentrations and is the best choice for diagnosis of autoimmune thyroid disease.³

Prospective studies of women with subclinical hypothyroidism have shown rates of progression ranging from approximately 3% to 8% per year, with the higher rates seen in individuals with initial TSH concentrations greater than 10 mU /L and in those with positive TPO-Ab.⁴ Subclinical hypothyroid patients with high titre of Anti thyroid peroxidase antibodies are more likely to progress to overt hypothyroidism.⁵

Thyroid disorders are very common endocrinological problem in clinical practice. Autoimmunity as a cause of hypothyroidism is a well-known fact, but prevalence of Anti thyroid antibodies and hypothyroidism in our part of country is not well documented. Therefore this study aimed in determining the prevalence of anti thyroid peroxidase antibody in overt and subclinical hypothyroidism and its relation with respect to age, sex, clinical features and thyroid function test of patients.

2. METHODOLOGY

This study was a hospital based, observational, cross sectional study. It was conducted for a duration of 1 year between August 2015 to August 2016. The ethical clearance for the study was obtained from the Institutional Review Board (IRB) of NAMS before the starting of the study. Sample size calculated by using following formula: $n = Z^2PQ/d^2$, Where n = required sample size, Z = z deviated corresponding to desired reliability level (1.96), P= estimated prevalence in the population (12.76%)⁶, Q = 100-P (if P is in %), d = maximum tolerable error (9%), there fore the required sample was 50 for the study.

Clinically screened patients of >18years with biochemical evidence of newly diagnosed primary hypothyroidism including subclinical hypothyroidism were included in the study. Those females in gestational or postpartum period, patients with radioactive iodine or surgery, medications like amiodarone, lithium, anti thyroid drugs etc were excluded from the study. Detailed history and thorough clinical examination was done as per pre-structured pro-forma. Thyroid stimulating hormone (TSH), free thyroxine (fT4) and free triiodothyronine (fT3) were measured with Chemiluminescence Assay. Anti TPO was done by Electro-chemiluminescence immuno assay (ECLIA-COBAS normal range <34IU/mL). Diagnosis of hypothyroidism was made based on higher than normal TSH (>4.68 μ IU/ml)and low fT4 (<0.78 ng/dl) \pm clinical symptoms or signs.

Statistical analysis was performed using SPSS 16. Each continuous parameter between the two groups, patients with subclinical hypothyroidism and overt hypothyroidism were analyzed using two tailed Chi square test. Means between various age groups and TSH were analyzed by one way anova test. Data was re-explored using the cut off value. P-value of less than 0.05 was considered significant. Multivariate analysis of variables with significant correlation was carried out. Ninety-five percent confidence intervals (CIs) were used in all analyses.

3. RESULTS

In this study, a total of 50 patients of newly diagnosed primary hypothyroidism visiting Bir hospital, Kathmandu in the time period of 1 year were included. History, examination and routine investigations along with Anti TPO antibody were done for every patient. Among the 50 patients of primary hypothyroidism, 15 were male (30%) and 35 were female (70%) i.e. more than double number of male patients.

Table 1: Age wise distribution of patients.

| Age group | Frequency (n) | Percentage (%) |
|-----------|---------------|----------------|
| 18-29 | 14 | 28.0 |
| 30-39 | 10 | 20.0 |
| 40-49 | 13 | 26.0 |
| 50-59 | 10 | 20.0 |
| >60 | 3 | 6.0 |
| Total | 50 | 100.0 |

Table 2: Distribution of Severity of hypothyroidism.

| Severity | Frequency(n) | Percentage(%) |
|----------------------------|--------------|---------------|
| subclinical hypothyroidism | 22 | 44.0 |
| overt hypothyroidism | 28 | 56.0 |
| total | 50 | 100.0 |

Table 3: TPO Distribution.

| Anti TPO status | Frequency(n) | Percentage (%) |
|------------------------|--------------|----------------|
| Negative(<34) | 36 | 72.0 |
| Positive (≥ 34) | 14 | 28.0 |
| Total | 50 | 100.0 |

Table 4: Prevalence of classical symptoms and signs of hypothyroidism in the TPO Ab positive and TPO Ab negative groups. n=50, $X^2= 3.84$ at df 1.

| Symptoms and signs | | TPO Status | | Chi square value | df | P value |
|--------------------|---------|------------|----------|------------------|----|---------|
| | | negative | positive | | | |
| Lethargy | absent | 21 | 9 | 0.145 | 1 | 0.700 |
| | present | 15 | 5 | | | |
| Cold intolerance | absent | 35 | 13 | 0.50 | 1 | 0.479 |
| | present | 1 | 1 | | | |
| Constipation | absent | 35 | 14 | 0.397 | 1 | 0.529 |
| | present | 1 | 0 | | | |
| Tingling sensation | absent | 31 | 11 | 0.426 | 1 | 0.514 |
| | present | 5 | 3 | | | |
| Anxiety | absent | 35 | 14 | 0.397 | 1 | 0.529 |
| | present | 1 | 0 | | | |
| Depression | absent | 36 | 14 | - | - | - |
| | present | 0 | 0 | | | |

| | | | | | | |
|--------------------|---------|----|----|-------|---|-------|
| Weight gain | absent | 21 | 9 | 0.149 | 1 | 0.700 |
| | present | 15 | 5 | | | |
| Hair fall | absent | 34 | 11 | 2,822 | 1 | 0.092 |
| | present | 2 | 3 | | | |
| Decreased appetite | absent | 36 | 14 | - | - | - |
| | present | 0 | 0 | | | |
| Insomnia | absent | 36 | 14 | - | - | - |
| | Present | 0 | 0 | | | |
| Menorrhagia | absent | 31 | 10 | 1.472 | 1 | 0.225 |
| | Present | 5 | 4 | | | |
| Dry skin | absent | 35 | 14 | 0.397 | 1 | 0.529 |
| | Present | 1 | 0 | | | |
| Facial puffiness | absent | 28 | 11 | 0.004 | 1 | 0.95 |
| | Present | 8 | 3 | | | |
| Non pitting edema | absent | 22 | 11 | 1.369 | 1 | 0.242 |
| | present | 14 | 3 | | | |
| Neck swelling | absent | 29 | 10 | 0.489 | 1 | 0.484 |
| | present | 7 | 4 | | | |
| Bradycardia | absent | 36 | 14 | - | - | - |
| | present | | | | | |

Table 5: TPO status with age.

| TPO status | Frequency | Mean Age | Std. deviation | P value |
|------------|-----------|----------|----------------|---------|
| Negative | 36 | 39.83 | 14.33 | 0.288 |
| positive | 14 | 44.35 | 10.26 | |

Table 6: Relation of TPO Anti bodies in hypothyroid patient. ($X^2=3.84$, 5.99 at df 1 and 2 respectively).

| Age group (years) | TPO negative(n) | TPO positive(n) | Chi square value | df | P value |
|-------------------|-----------------|-----------------|------------------|----|---------|
| | | | | | |

| | | | | | |
|---------------------------|----|----|-------|---|-------|
| 18-29 | 13 | 1 | 7.352 | 2 | 0.118 |
| 30-39 | 6 | 4 | | | |
| 40-49 | 9 | 4 | | | |
| 50-59 | 5 | 5 | | | |
| ≥60 | 3 | 0 | | | |
| Sex | | | | | |
| Female | 22 | 13 | 4.83 | 1 | 0.028 |
| Male | 14 | 1 | | | |
| Hypothyroid Status | | | | | |
| Sub clinical | 16 | 6 | 0.010 | 1 | 0.919 |
| overt | 20 | 8 | | | |
| TSH level | | | | | |
| 4.68- 10 | 19 | 5 | 1.176 | 1 | 0.278 |
| >10 | 17 | 9 | | | |

Among female, 13(37%) out of 35 were positive for Anti TPO Ab, while only 1(6.67%) out of 15 male were positive for Anti TPO Ab so female patients were more likely to be TPO positive which was statistically significant (p value=0.028). TPO positive patient in subclinical hypothyroidism was 6(27.3%) out of 22 while in overt hypothyroidism it was 8(28.6%) out of 28. Which was almost similar and statistically not significant. TPO positive patients were 9(35%) out of 26 in high TSH group (TSH=>10) where as it was 5(21%) out of 24 patients having low TSH level (4.68-10).Which was not statistically significant.

Table 7: TPO status with relation to TSH.

| TPO status | frequency | Mean TSH | Std. deviation | P value |
|------------|-----------|----------|----------------|---------|
| Negative | 36 | 13.39 | 15.53 | 0.037 |
| positive | 14 | 26.61 | 27.68 | |

Mean TSH was higher in TPO positive group as compare to TPO negative group which was statistically significant ($p=0.037$)

4. DISCUSSION

Hypothyroidism is common endocrine dysfunction in Nepalese population. In this study 50 patients of primary hypothyroidism those diagnosed first time were evaluated and examined along with relevant investigation. Among them 35 (70%) were female and 15(30%) were male revealing that prevalence of hypothyroidism was more common in female than male. Similar study done in pokhara by Paudel K and Paudel B revealed similar result where among 88 patients 13 were male and 75 were female.⁷ A retrospective study done in Pokhara Charak hospital, out of 1504 general population, 1155 were females and 349 were males. The prevalence of hypothyroidism in western part of Nepal was about 12.07% and female had higher prevalence of thyroid dysfunction than male.⁶ In this study maximum number of patient those were enrolled in the study were in the range of 18-29, followed by age group of 40-49 which suggested that younger and middle age population were affected more with mean age of patients was 41.1 year. While study done in University of Texas-Houston Medical School among 143 patients over the age of 18 years showed that mean age of hypothyroid patient was 43.4 (SD =13.0) year⁸ which was almost similar to our study.

This study showed that 22(44%) patients had subclinical hypothyroidism while 28(56%) patients had clinical hypothyroidism. While in contrast to this study the study done in Charak hospital pokhara, the prevalence of overt hypothyroidism was 2.26% and subclinical hypothyroidism was 10.50%.⁶ The most frequent signs and symptoms were lethargy, weight gain, facial puffiness, non pitting edema and neck swelling in this study. Another study from Pokhara showed that the most frequent symptoms were lethargy, cold intolerance, constipation, tingling sensation and weight gain, and the most frequent signs were facial puffiness and non-pitting pedal edema. which were almost similar to our study.⁷

In this study, among the total patients 28% had anti TPO antibody positive (6.67% among male and 37% among female). Mean age of TPO positive patient was 44.3 years vs. 39.8 years in TPO negative patient. This show that TPO positivity increases with increasing age. Mean TSH value was also significantly higher in TPO positive patients as compared to negative patients. This number was similar to other reported studies on hypothyroid patients including those with subclinical hypothyroidism. In the thyroid study done at Gandaki Medical College Teaching Hospital, 37.5% of hypothyroid patients had TPO antibody positive in which 41.3% were female and 15.4% male. Mean TSH in TPO positive patients was higher than in TPO negative patients while mean age was similar in both groups.⁷ In an Indian population based study, the prevalence of TPO antibody positivity was 16.7% in the studied population. Whereas, it was found to be 9.5% among subjects with normal thyroid function, and 53% among subjects with subclinical hypothyroidism.⁹ A study done in Saudi Arabia showed that 11% people living in Hail region of Saudi Arabia were suffering from Hashimoto thyroiditis. 20% of them were male and 80% female. About 37% of total population were positive for Anti-TPO assay with titer ranging from 5 to 600 IU/ml.¹⁰ In the United States Population (1988 to 1994) National Health and Nutrition Examination Survey (NHANES III), TSH and the prevalence of anti thyroid antibodies were greater in females, which increased with age, and were greater in whites and Mexican Americans than in blacks.¹¹

A longitudinal Study done in University of Texas-Houston Medical School showed that the prevalence of the anti TPO antibody in the high-normal group (2.5–5.49 IU/ml) was 18.6% versus 3% in the low-normal (0.36–2.49 IU/ml) range TSH. The anti TPO prevalence was higher in females than in males and had a racial predominance in Hispanics compared to African Americans; however, these differences were not statistically significant. Anti TPO measurement may be appropriate for patients with high-normal TSH to help distinguish those at risk of developing true hypothyroidism.⁸

A Danish study showed that, TPO Ab and/or Tg Ab was found in 95% of overtly hypothyroid patients.¹² The progression of subclinical hypothyroidism to clinical hypothyroidism has been estimated at 5% per year in a 4-year follow-up. The prevalence of anti TPO in the general population range from 4.4% to 25%. Greater prevalence of anti TPO antibodies suggest that these patients have a higher risk of developing overt hypothyroidism and they should have closer follow-up.¹³ TPO probably interfere with catalysis of thyroglobulin iodination in vivo which may be a cause of hypo function of the thyroid in patients with chronic thyroiditis.¹⁴ Thyroid study done in Chengdu, Sichuan

Province, China noted that the prevalence of thyroid autoantibodies in subclinical hypothyroidism and clinical hyper and hypothyroidism was significantly greater than in euthyroid subjects. The study had detected a significantly greater serum median TSH concentration in the participants who were positive for thyroid autoantibodies compared with those who were negative.¹⁵ Thus population positive for thyroid autoantibodies may be at a high risk of abnormal thyroid function. A routine examination of thyroid function in individuals with positive thyroid autoantibodies may be necessary and is suggested based on these current findings.

5. CONCLUSIONS

Significant Positive correlation was observed between patients with high serum TSH and TPO positive status. Female had high prevalence of TPO positivity as compared to the male which was statistically significant. Hashimoto's thyroiditis was a common cause of primary hypothyroidism, but often remain undiagnosed until thyroid antibodies were tested.

6. ACKNOWLEDGEMENT: None

7. Conflicts of interest: None

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