Research Article
Thyroid Profile among the Subjects from Fluorotic Zone – A Biochemical Perspective

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Abstract
Study aimed at assessing the thyroid function under the influence of high fluoride content in the water in fluorosis prevalent zones. In addition to bone and teeth soft tissue like thyroid gland were also shown to be affected as evident from the earlier studies. Fluoride can rapidly cross cell membrane in tissues that are metabolically active and hence the thyroid gland. Fluoride also interferes with Thyroid Stimulating Hormone (TSH) production and also the thyroid hormones free Triiodothyronine (FT₃) and free Thyroxine (FT₄).
Prakasam district in Andhra Pradesh is fluorosis prone zone and subjects visiting Government medical institution from these areas are chosen as subjects and blood samples were collected to study parameters of thyroid function tests [FT₃, FT₄ and TSH]. Fluoride levels of the water from the fluorotic zones and also in the serum of the subjects were estimated for the correlative study. Altered thyroid function was evident with low FT₃, FT₄ levels and high TSH levels. Concurrently high levels of fluoride were seen in the water samples from the concerned areas, the subjects hailing from. The results were statistically significant reflecting hypothyroid status in majority of the subjects in association with fluorosis as evident by high levels of fluoride in the water.

Keywords: Fluorosis, Thyroid Concentration, Thyroid Function tests, Hypothyroidism.

Introduction
Though thyroid gland takes up iodine for thyroid hormone synthesis other halogens like fluoride can easily replace the iodine interfering with the thyroid production by virtue of its low atomic weight[1]. On this scenario in fluorosis prevalent zone the lively hood of thyroid dysfunction is high. Current study aims at assessing the thyroid
function by estimating parameter like FT$_3$, FT$_4$ and TSH. Due to competitive inhibition of iodine by fluoride thyroid production is seriously interfered. This thyroid dysfunction can even influence the IQ levels of growing children, miscarriage in pregnant women and pathocytological changes in individuals affected$^{[2-4]}$. FT$_3$, FT$_4$ levels for conforming to the hypothyroid status. This is also reflected in high levels of TSH. Fluoride levels of even 1 mg/L in water was shown to have deleterious effect on thyroid function as shown in the study carried out by Basha et al$^{[5]}$. Many areas in Prakasam district using ground water as primary water source found to have high levels of fluoride in water. High fluoride ingestion from various sources is found with anomalous thyroid capacity in both animals and people with low dimensions of thyroid hormones and high TSH production. A few investigations detailed a decrease in the FT$_4$ and FT$_3$ levels just as an anomalous increase in the TSH levels$^{[6-11]}$.

Methods
The study was conducted to evaluate and correlate the effect of chronic excess fluoride intake on thyroid function among subjects residing in fluorotic prone zones. The villages with high fluoride levels in the drinking water in the Prakasam district of Andhra Pradesh, India were included. This study was aimed at determining the correlation between fluoride levels in the drinking water, hormones of thyroid gland in fluorosis prone zones of Prakasam district of Andhra Pradesh. All the methods were carried out in accordance with the relevant guidelines and regulations. A total of 342 subjects included in the study sparing for one year from October 2016 to August 2018. To ensure that the subjects are from the fluorosis prone zone, water samples from the areas in question are collected for analyzing fluoride levels. The samples of drinking water were collected in plastic bottles. Fluoride determination in the drinking water was carried out by using spectrophotometrically by SPADNS method. Irrespective of the age and sex blood samples are obtained from the subjects hailing from the established fluorotic zones and blood samples were left to clot at room temperature by centrifugation serum was separated for assessing the thyroid hormones and TSH in correlation with the fluoride content of the potable water in the respective areas. Following the ethical committee approval the serum samples were investigated to assess FT$_4$, FT$_3$ and TSH hormone levels using Immuno Chemiluminescence Microparticle Assay (ICMA) with the Bayer Centaur Auto Analyzer. These samples were collected from the patients attending to institutional hospital that caters to the medical needs of the neighboring fluorosis prone areas. The subjects from fluorotic zone with or without thyroid dysfunction were included in the study and the subjects with pre-existing thyroid disorders with supplementation of thyroxine were excluded.

Results
Majority of the water samples found to show fluoride levels of more than 1.5 mg/L from the areas chosen for the study, that are said to be fluorosis prevalent zones. Serum fluoride levels among the subjects were variable; some showing normal levels while others with relatively high value. Parameters of thyroid function test namely FT$_3$, FT$_4$ were found to be low in the most of the subjects, while TSH is found to be raised reciprocally. FNAC picture showed varied pathological entities with respective cytomorphological changes ranging from euthyroid to hashimoto’s thyroiditis, lymphocytic thyroiditis, autoimmune thyroiditis, adenomatous goitre, nodular goitre, colloid goitre and follicular adenomas.
Fig 1: Number of affected cases in association with varied pathological entities affecting thyroid gland

Table 1: Mean FT₃ levels in association with varied pathological entities affecting thyroid gland

| Pathological Entity                  | N  | Mean   | Std. Deviation | P Value     |
|--------------------------------------|----|--------|----------------|-------------|
| Euthyroid                            | 42 | 3.0595 | 0.84191        |             |
| Hashimoto's thyroiditis              | 105| 1.9806 | 0.6588         |             |
| Lymphocytic thyroiditis              | 33 | 1.6939 | 0.29889        |             |
| Autoimmune thyroiditis               | 25 | 2.148  | 1.13739        | < 0.005     |
| Adenomatous goitre                   | 48 | 3.2392 | 0.43412        |             |
| Nodular goitre                       | 48 | 3.0188 | 0.3228         |             |
| Colloid goitre                       | 26 | 3.55   | 0.9542         |             |
| Follicular adenoma                   | 15 | 3.1807 | 0.38734        |             |
| Total                                | 342| 2.5920 | 0.9416         |             |

Table 2: Mean FT₄ levels in association with varied pathological entities affecting thyroid gland

| Pathological Entity                  | N  | Mean   | Std. Deviation | P Value     |
|--------------------------------------|----|--------|----------------|-------------|
| Euthyroid                            | 42 | 1.0531 | 0.4293         |             |
| Hashimoto's thyroiditis              | 105| 0.7351 | 0.4191         |             |
| Lymphocytic thyroiditis              | 33 | 0.3618 | 0.1912         |             |
| Autoimmune thyroiditis               | 25 | 0.6872 | 0.5446         |             |
| Adenomatous goitre                   | 48 | 1.2656 | 0.1930         | < 0.005     |
| Nodular goitre                       | 48 | 1.1131 | 0.5125         |             |
| Colloid goitre                       | 26 | 1.3369 | 0.1203         |             |
| Follicular adenoma                   | 15 | 1.1407 | 0.1285         |             |
| Total                                | 342| 0.9257 | 0.4768         |             |

Table 3: Mean TSH levels in association with varied pathological entities affecting thyroid gland

| Pathological Entity                  | N  | Mean   | Std. Deviation | P Value     |
|--------------------------------------|----|--------|----------------|-------------|
| Euthyroid                            | 42 | 3.73   | 0.83977        |             |
| Hashimoto's thyroiditis              | 105| 73.6494| 15.22764       |             |
| Lymphocytic thyroiditis              | 33 | 50.9712| 3.22752        |             |
| Autoimmune thyroiditis               | 25 | 67.234 | 17.05413       |             |
| Adenomatous goitre                   | 48 | 3.794  | 0.8797         |             |
| Nodular goitre                       | 48 | 5.0481 | 2.46212        |             |
| Colloid goitre                       | 26 | 3.7965 | 0.94728        |             |
| Follicular adenoma                   | 15 | 3.3707 | 0.2719         |             |
| Total                                | 342| 34.5802| 33.9992        |             |
Discussion
Fluoride and iodine being halogens, fluoride has got the higher tendency for the uptake by the thyroid gland rather than iodine, fluoride being lighter element\(^1\) with respective with atomic weight. Thus the higher activity of the fluoride is attributable to its low atomic weight that could replace the iodine leading to pathophysiological disturbances pertaining to the thyroid gland. Fluoride also has got deleterious effect on THS output by the pituitary gland and also competes with the THS receptor sites on thyroid gland consequently the impaired mechanism resultant are low THS by pituitary, reduced responsiveness of the thyroid gland by TSH and also reduce the thyroid production as iodine uptake is interfered\(^{12}\) Physiologically active FT\(_3\) component is obtained from FT\(_4\) by the activity of deiodinase, whose action is again interfered with by fluoride leading to low fraction of physiological thyroid. Among the subjects screened for the thyroid profile FT\(_3\) levels were as low as 0.7 pg/ml and highest recorded value being 4.1 pg/ml [Table 1]. on the same lines lowest FT\(_4\) measured was 0.08 ng/ml and highest value obtained 1.65 ng/ml [table 2]. Similarly lowest recorded TSH value was 3.35 µIU/ml while the highest among the subjects being 73.654 µIU/ml [Table 3]. The most significant finding is obtained in the data is more than 30% of the cases were found to be associated with the Hashimoto’s Thyroiditis and the same group has shown the TSH levels ranging from 52 µIU/ml as high as 115 µIU/ml reflecting the compromised thyroid secretion. 12.2 % of cases were euthyroid and obvious hypothyroid status was seen in 45% of the cases with co-existing autoimmune thyroid disorders\(^{13,14}\). A small proportion of the cases were found in association with malignancy of follicular adenoma. Little more than 35% of the cases were found in association with the goitre. The core of the study being fluorosis, the fluoride levels of the water estimated was ranging between 0.23 mg/L and 12.7 mg/L justifying the selection of subjects as they hail from this fluorosis established areas. Serum fluoride levels ranging from 0.144 to 1.546 mg/L that was correlative with high fluoride levels of water from the concerned area. In addition to thyroid profile cytological study by way of FNAC was also carried out to supplement to the findings of thyroid function test parameters. Majority of the cases were found in association with various pathological entities of thyroid gland [15].

Conclusion
The current study highlights deranged functions of thyroid reflected in attend thyroid biochemical parameters in the presence of high fluoride content in the water in their environment. It is desirable to examine the thyroid function of the people attending to the outpatient department under given scenario in the light of knowledge of affliction of thyroid function by fluoride.

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