Original Article

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Biochemistry Section

Prevalence of Thyroid Disorders in and around Nalgonda District, Telangana, India: A Cross-sectional Study

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ABSTRACT

Introduction: Among the endocrine disorders, thyroid disorders are the most common. Long term and excessive intake of fluoride plays a significant role in the development of thyroid disorders. Nalgonda is one of the highly drought-prone districts in Southern India and its groundwater has 10-15 parts per million (ppm) of fluoride in contrast to a maximum permitted level of just 1.5 ppm. The entire Nalgonda division is under the threat of fluorosis due to high concentration of fluoride in the drinking water.

Aim: To assess the prevalence of thyroid disorders in and around areas of Nalgonda district, Telangana, India.

Materials and Methods: A cross-sectional study was conducted in Department of Biochemistry, Government Medical College, Nalgonda, Telangana, India, from December 2021 to May 2022. Total 391 subjects attending Outpatient Department (OPD) of General Medicine, Nalgonda were included in the study. Samples were analysed for thyroid function tests (total T3,T4, thyroid stimulating hormone) by chemiluminiscence immuno assay method in an Abbott architect ci4100 automated analyser. Statistical analysis was done by using Microsoft excel spreadsheets and results were expressed as prevalence percentages, mean±Standard Deviation (SD).

Results: In the present study, the mean age was 39.5±20.506 years. Out of the total participants, 273 (69.8%) subjects were found to be euthyroid and 118 (30.2%) had thyroid disorders. Among 30.2% subjects with thyroid disorders, 32 (8.2%) were hypothyroid, 19 (4.9%) were hyperthyroid, 54 (13.8%) were having subclinical hypothyroidism, 13 (3.3%) were having subclinical hyperthyroidism. The prevalence of thyroid disorders was higher in females compared with males, with the ratio of 3:1 and females contributing to major disease burden.

Conclusion: According to this study, prevalence of thyroid disorders was 30.2% with more disease burden in females. Subclinical hypothyroidism contributes to the major disease burden.

Keywords: Fluorosis, Hypothyroidism, Sodium iodide symport transporter, Thyroid dysfunction

INTRODUCTION

Among endocrine disorders, thyroid disorders are the most common disorders. Gender, age, ethnicity, geographical factors and iodine intake are factors that govern the prevalence and pattern of thyroid disorders [1].

The thyroid is a small, butterfly-shaped gland located at the anterior region of the neck, synthesises and secretes two hormones i.e., T4 (Thyroxine) and T3 (Triiodothyronine) under stimulation of Thyroid Stimulating Hormone (TSH) produced by the pituitary gland to synthesise and release the thyroid hormones into the blood [2].

Flourosis is one of the important public health problems in India. Fluoride is an element that occurs either naturally in the environment or can be industrialised and added artificially to public drinking water [3]. A concentration of 0.5-0.8 ppm of fluorine in drinking water is considered as safe limit in india [4]. The upper admissible limit of fluoride in drinking water is 1.5 mg/L as per Bureau of Indian Standards (BIS) [5] beyond which it is called as fluoride toxicity. In Flouride toxicity and flourosis it was proven that high maternal and infant mortality rate also could be due to consumption of fluoride salts through variety of sources which interfered with nutrient absorption, decreased thyroid hormone production. Literature reported potential association between fluoride exposure to endocrine diseases [5].

Fluoride acts to inhibit Na^+, K^+-ATPase activity, which is essential for regulating Sodium Iodide Symporter (NIS) functionality. Diverse lines of evidence demonstrate that Flouride inhibits NIS expression and functionality thereby contributing to impaired iodide absorption, diminished iodide-concentrating ability and iodine deficiency disorders. Evidence has been presented that Tumour Necrosis Factor (TNF)-α, Transforming Growth Factor (TGF)-β1, Interleukin (IL)-6 and IL-1β, Interferon (IFN)-γ, Insulin-like Growth Factor (IGF)-1, Phosphoinositide 3-kinase (PI3K) and Tg inhibit NIS expression and that fluoride upregulates TNF-α, TGF-β1, IL-6 and IL-1β, IFN-γ, IGF-1, PI3K and Tg expression and activity [6].

The factors for higher incidence of fluoride in groundwater resources include the lock of freshwater exchange due to periodical droughts, the granites and the arid climate of the Nalgonda region [7]. Similar studies done by Sashi A and Singla S [8], Singh N et al., [9], Shaik N et al., [10] to evaluate the effect of dental and skeletal fluorosis in children, were conducted in urban areas and other parts of India, but there is paucity of data from rural areas of Telangana, India. Hence present study was conducted to assess the thyroid status in and around the areas of fluorosis affected Nalgonda district, Telangana.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Biochemistry, Government Medical College, Nalgonda, Telangana, India, from December 2021 to May 2022 for a period of six months after obtaining the Institutional Ethical Committee clearance (IEC no: GMC/NLG/IEC/8/2021).

Inclusion criteria: Individuals aged between 18-60 years, from the population in and around areas of Nalgonda, who were attending OPD of General Medicine, Government General Hospital/ Government Medical College, Nalgonda, Telangana, India after obtaining verbal consent were included in the study.

Exclusion criteria: Patients with diabetes mellitus, females with pregnancy and lactation and subjects who were not willing to participate in the study were excluded from the study.

Sample size calculation: Sample size was calculated using Andrews fischer formula [11]:

$n=z^2pq/d^2$

where, n- sample size

z=Z score

p=prevalence

q=(1-p)

d=confidence interval

With 95% confidence level and prevalence of 40%, considered based on a study by Vinodh B et al., [12], final sample size calculated was 368.

Study Procedure

Demographic data (age, gender) were collected from all the study participants. After obtaining verbal consent from all the participants, 5 mL of fasting blood samples (overnight fasting for about 8-10 hours) from 391 subjects were collected in red vacutainers, samples were centrifuged at 5000 Revolutions Per Minute (RPM) at 37°C for 5 minutes and were analysed for thyroid function tests (total T3,T4,TSH) in an Abbott architect ci4100 automated analyser by chemiluminiscence immuno assay method and results were analysed. Reference ranges were taken from abott architect ci 4100 manufacturing kit inserts. The laboratory reference ranges of thyroid function tests are given in [Table/Fig-1].

Parameters	Reference interval
TSH	0.35-4.94 µIU/mL
Total T3	0.35-1.93 ng/mL
Total T4	4.87-11.72 µg/dL

[Table/Fig-1]: Reference intervals of thyroid function tests.

Subjects were categorised according to measurements of serum TSH and total thyroid hormone (T3 and T4) concentrations as follows [13]:

Hyperthyroidism was classified as overt, if level of serum TSH was <0.35 µIU/mL with raised total T4 and total T3 or raised total T3 alone (T3-toxicosis) and subclinical hyperthyroidism if serum TSH level was <0.35 µIU/mL with normal total T4 and total T3. The criteria for euthyroidism include serum TSH 0.35-4.94 µIU/mL with normal T3 and T4. Hypothyroidism was classified as subclinical if serum TSH level was >4.94 µIU/mL with normal total T4 and T3 and overt if serum TSH >4.94 µIU/mL with low total T4 and T3.

STATISTICAL ANALYSIS

The demographic categorical data and results were codified in Microsoft excel spread sheets and analysis done by necessary statistical tests, expressed as prevalence percentages, (Prevalence%= total number of diseased/total number of study population), mean±SD, and represented as tables using graph pad prism version 9.0.

RESULTS

In the present study, among the total 391 study population, females were 200 and 191 were males with a mean age was 39.5±20.50 years. Maximum patients in present study were aged between 51-60 years [Table/Fig-2].

Age (years)	Gender		Total
	Male	Female	
18-30	44	53	97
31-40	49	48	97
41-50	50	45	95
51-60	48	54	102
Total	191	200	391

[Table/Fig-2]: Age and gender wise distribution of study subjects.

In the present study, in the euthyroid group, the mean level of serum TSH was 1.92±0.11 µIU/mL, total T3 was 0.99±0.21 ng/mL, total T4 was 6.84±0.31 µg/dL. In the hypothyroid group, the mean level of serum TSH was 8.4±1.8 µIU/mL, total T3 was 0.28±0.02 ng/mL, total T4 was 3.47±1.2 µg/dL. In the hyperthyroid group, the mean level of serum TSH was 0.18±0.02 µIU/mL, total T3 was 2.6±0.3 ng/mL, total T4 was 12.8±0.4 µg/dL [Table/Fig-3].

Mean value	Euthyroid	Hypothyroid	Hyperthyroid
TSH (µIU/mL)	1.92±0.11	8.4±1.8	0.18±0.02
T3 (ng/mL)	0.99±0.21	0.28±0.02	2.6±0.3
T4 (µg/dL)	6.84±0.31	3.47±1.2	12.8±0.4

[Table/Fig-3]: Mean values of thyroid parameters in euthyroid and thyroid disorders.

Subjects were stratified based on their age into four groups and analysed for prevalence of thyroid disease in the groups [Table/Fig-4].

The distribution of thyroid disorders was tabulated according to age, where, out of total thyroid disorders 38 (9.7%) were between 18-30 yrs, 35 (9%) were 31-40 yrs, 26 (6.7%) were 41-50 yrs and 19 (4.8%) were 51-60 yrs. The prevalence of thyroid dysfunction was higher in the age group <40 yrs of age than compared with >40 yrs of age. Total 113 (28.9%) females were found to be euthyroid and 87 (22.2%) having thyroid dysfunction contributing to 22.2% of disease prevalence. In 191 males, 160 (40.9%) were euthyroid and 31 (7.9%) were with thyroid disorders contributing to 7.9% of disease prevalence. The prevalence of thyroid disorders was high in females compared with males in the ratio of 3:1 with females contributing to major disease burden [Table/Fig-5].

In the present study out of 391 subjects, 273 (69.8%) were found to be euthyroid, and 118 (30.2%) had thyroid disorders. Among subjects with thyroid disorders, 32 (8.2%) were having hypothyroid, 19 (4.9%) were hyperthyroid, 54 (13.8%) were in subclinical hypothyroidism, 13 (3.3%) were in subclinical hyperthyroidism. Hypothyroidism was more prevalent (22%) than hyperthyroidism [Table/Fig-6].

Age (years)	Total		Euthyroid (n)		Total %	Thyroid disorders (n)		Total %	Hypothyroid				Hyperthyroid			
	Male	Female	Male	Female		Male	Female		Clinical (n)	%	Subclinical (n)	%	Clinical (n)	%	Subclinical (n)	%
18-30	44	53	32	27	15.08	12	26	9.71	11	2.81	17	4.34	5	1.27	5	1.3
31-40	49	48	39	23	15.85	10	25	8.95	10	2.55	15	3.83	6	1.53	4	1
41-50	50	45	45	24	17.64	5	21	6.64	8	2.04	12	3.06	4	1.02	2	0.5
51-60	48	54	44	39	21.22	4	15	4.85	3	0.76	10	2.55	4	1.02	2	0.5
Total	191	200	160	113	69.79	31	87	30.15	32	8.16	54	13.78	19	4.84	13	3.3

[Table/Fig-4]: Represents the summarised data of study population.

Age (years)	Euthyroid		Hyperthyroid		Hypothyroid	
	Male n (%)	Female n (%)	Male n (%)	Female n (%)	Male n (%)	Female n (%)
18-30	32 (8.18)	27 (6.9)	4 (1.02)	6 (1.5)	8 (2.04)	20 (5.1)
31-40	39 (9.97)	23 (5.8)	4 (1.02)	6 (1.5)	6 (1.5)	19 (4.9)
41-50	45 (11.5)	24 (6.1)	2 (0.5)	4 (1.02)	3 (0.7)	17 (4.3)
51-60	44 (11.2)	39 (9.97)	2 (0.5)	4 (1.02)	2 (0.5)	11 (2.8)

[Table/Fig-5]: Overall prevalence of euthyroid and thyroid disorders.

Age (years)	Hypothyroid				Hyperthyroid			
	Overt n (%)		Subclinical n (%)		Overt n (%)		Subclinical n (%)	
	Male	Female	Male	Female	Male	Female	Male	Female
18-30	3 (0.77)	8 (2.04)	5 (1.28)	12 (3.07)	2 (0.5)	3 (0.77)	2 (0.5)	3 (0.77)
31-40	2 (0.5)	8 (2.04)	4 (1.02)	11 (2.8)	2 (0.5)	4 (1.02)	2 (0.5)	2 (0.5)
41-50	1 (0.25)	7 (1.8)	2 (0.5)	10 (2.6)	1 (0.25)	3 (0.77)	1 (0.25)	1 (0.25)
51-60	1 (0.25)	2 (0.5)	1 (0.25)	9 (2.3)	1 (0.25)	3 (0.77)	1 (0.25)	1 (0.25)

[Table/Fig-6]: Gender and Age-wise distribution of thyroid disorders.

DISCUSSION

Thyroid disorders are one of the commonest endocrine dysfunction worldwide. In India hypothyroidism contributes to high prevalence percentage of total thyroid diseases [14].

The present study revealed that prevalence of thyroid dysfunction contributing to disease burden was 30.2% of the studied population. In the studies conducted in Mumbai by Desai PM [15] thyroid disease prevalence was 26% which is similar to this study.

The most common thyroid disorder observed was subclinical hypothyroidism (13.8%) followed by clinical hypothyroidism (8.2%), hyperthyroidism (4.9%) and subclinical hyperthyroidism (3.3%). Present study findings are similar with the studies conducted by, Kumar D et al., (13.3%) [16], Rashad NM and Samir GM, (65%of thyroid disorders) [17], Marwaha RK et al., (23%) [18], Nouh AM et al., (7.3%) [19], Lamfon HA (47.3%) [20], Vinodh B et al., (33%) [12], Jalikhani R et al., (38%) [21], Sandeep S et al., (37.2%)[22] and few other Indian and international epidemiological studies are tabulated in [Table/Fig-7] [12,13,17,23-26].

Study by Sandeep S et al., concluded that the subclinical hypothyroidism was the major underlying dysfunction for which the probable cause could be excess flouride in drinking water. A linear correlation with raised TSH levels was demonstrated with excess of fluoride in drinking water, most of which were subclinical cases [22].

Study by Sinmahapatra P et al., comparing the effect of flouride on functioning of thyroid in endemic and non endemic areas revealed total cases of hypothyroidism (subclinical and overt) in endemic and non endemic region were 34% (27+7%) and 20%(17+3%) respectively, showing significant proportionate distribution of hypothyroid cases higher in endemic with respect to non endemic areas as fluoride hinders secretion of thyroid hormones along with directly damaging thyroid follicles [23].

Peckham S et al., study also stated that Flouride in drinking water provides a useful contribution for predicting prevalence of hypothyroidism [27]. In a study by Kumar V et al., Maharshtra, it was evident that positive correlation existed between fluorosis and thyroid functional activity and excessive fluoride levels lead to alteration in thyroid hormones activity [28].

In a study by Chaterjee S et al., at West Bengal, it was shown that fluorosis can affect thyroid gland resulting in hypothyroidism and it disclosed a significant correlation between the thyroid hormone level and serum fluoride concentration which enhances the fact of a clear relationship in between them [24].

In a similar study by Singla S and Shashi A, in Punjab, it showed that the ingestion of drinking water with high concentration of fluoride leads to stress of the mechanism of biosynthesis of thyroid hormones, as evidenced by depletion in the activity of Thyro Peroxidase (TPO), which may be produced by the attraction of fluoride with oxidised form of iodide and/or with the iodide site on the TPO molecule. This tends to decrease in the concentration of T3, T4 and increase production of TSH in the serum [29].

Hypothyroidism is a major health problem concern and in addition to other factors such as iodine deficiency, fluoride exposure should be considered as a contributing factor.

In the epidemiological study by Unnikrishnan AG conducted in eight cities of India, a significantly higher prevalence of hypothyroidism of Hyderabad city was tabulated concluding autoimmune mechanism appears to play an etiological role and iodine intake ceases to be a sole etiological contender for thyroid disorders in urban areas [30].

In an another study done by Marwaha RK et al., on countrywide screening of goitrous healthy young girls in India, it was seen that in patients with Fine Needle Aspiration Cytology (FNAC)-proven juvenile autoimmune thyroiditis, subclinical hypothyroidism was seen in 15% cases, thus concluding the role of autoimmunity in subclinical hypothyroidism [31] and is in same prevalence with the present study.

Present study showed that prevalence of thyroid dysfunction was high in the females (22.3%) compared to males (7.9%) with the affected ratio of 3:1 respectively. In a study by Nair A et al., significantly high prevalence of hypothyroidism was found in females, which is a known fact among non diabetic persons also [32]. Study conducted by Tunbridge et al., at Wickham survey incorporated in table show predominance of females affected by thyroid disorders than males [33]. In another study by Bhat N et al., it was concluded that women of 18-35 year age group are highly prone to develop thyroid disorders [25].

The prevalence of thyroid dysfunction was higher in the age group <40 years of age than compared with >40 yrs of age. In

Author of the study	Place and year of study	Thyroid disorder prevalance	Subclinical hypothyroidism (%)	Hypothyroidism (%)	Hyperthyroidism (%)
B Vinodh et al.,[12]	Andhra Pradesh [2013]	40	22.14	10.57	7.28
Jalikhani R et al., [21]	Jammu and Kashmir [2015]	40.36	33	5	1.6
Tayal D et al., [13]	Delhi [2012]	15	10.55	2.65	1.22
Sandeep S et al., [22]	Agra, Uttar Pradesh [2015]		37.2	58.3	50
Sinhapatra P et al., [23]	West Bengal [2009]		27	7	
Chaterjee S et al., [24]	Bankura [2016]		14.29 (subclinical+clinical)		
Rashad NM and Samir GM [17]	Egypt [2019]	29.30%	44.4	20.6	35
Bhat N et al., [25]	Nepal [2022]	16.66	14	1.8	0.6
Ahmed I et al., [26]	Pakistan [2022]		12.4 (subclinical+clinical)		1.6
Current study	Telangana [2022]	30.2	13.8	8.2	8.2

[Table/Fig-7]: Indian and International Epidemiological studies [12,13,17,21-26].

a retrospective study by Nagarker R et al., the prevalence of thyroid disorders was high in the age group <30 yrs than the group >30 yrs [34]. In Deshmukh V et al., study screening for subclinical hypothyroidism needs to be considered in perimenopausal females in view of raised thyroid autoimmunity after the age of 35 years [35]. A review study by Kostoglou-Athanassiou I and Ntalles K, concludes chronic auto immune thyroiditis affects three to five times more frequently women than men, usually middle-aged or older as well as children contributing to hypothyroidism [36].

In contrast to the present study, according to a study by Shaik N et al., [10] in Mysuru, Karnataka, showed that long term intake of naturally fluoridated drinking water (within the range of 0.02-1.4 ppm) doesn't seem to have any effect on the thyroid function in the children with normal nutritional status and optimal iodine intake.

A study by Michael M et al., at Ahmedabad, revealed that thyroid hormone levels do not vary in fluorotic individuals which is in contrast to the present study [37]. According to study by I Ahmed et al., Pakistan, in contrast to the present study, drinking water with raised fluoride level was found to have no effect on thyroid profile [26]. A study conducted by Barberio AM et al., in Canada, found that at the population level, fluoride exposure is not associated with impaired thyroid functioning in a time and place where multiple sources of fluoride exposure, including community water fluoride, exist which is in contrast with the present study [38].

In an another contrast study by Hosur MB et al., results did not show any significant alterations in the levels of the thyroid hormones free T3, free T4, and TSH in subjects with dental fluorosis [39].

Subclinical hypothyroidism contributes more towards the disease burden. Co-morbidities like cardiovascular and pregnancy complications, needs an attention on autoimmunity which might be a cause for hypothyroidism other than fluoride to prevent the impairment of activities, quality of life and economic productivity of the individual.

Limitation(s)

Limitations of the present study was inability to estimate serum fluoride and TPO antibody levels due to financial constraints to establish causal relationship.

CONCLUSION(S)

Hypothyroidism was highly prevalent (22%) among thyroid diseases with subclinical hypothyroidism contributing to majority of disease burden in and around areas of fluoride affected Nalgonda. Economical and reproductive age group was highly affected involving more females. Further studies for identification of risk factors, etiological contender, causal relationship and effects of other confounders involving more number of sample size and other investigations like serum fluoride, TPO antibodies is recommended to know the causal relationship of thyroid dysfunction.

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