Original Research Article

Spectrum of thyroid disorders in tertiary care hospital at Patancheru, Sangareddy, Telangana, India - A clinical study

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Abstract

Malnutrition, particularly iodine deficiency, is one of the major contributing factors to thyroid disorders in India. Poverty in India is contributing to the increase of thyroid disorders through malnutrition, poor sanitation, and lack of access to medical facilities. Another factor is the lack of awareness about the symptoms and risk factors of thyroid disorders. Intake recommendations for iodine are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies. WHO recommends universal iodinization of salt. High levels of iodine intake sometimes are associated with an increased risk of hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. We conducted a retrospective study at our hospital from December 2017 to January 2023. A total number of 57 cases were studied. Out of 57 patients, 46 patients presented with hypothyroidism and 11 with hyperthyroidism. Various clinical presentations, pathologies and socioeconomic problems are discussed.

Key words

Iodine, Hyperthyroidism, Hypothyroidism, Malnutrition, Poverty, Health Access, Health Awareness, Universal Iodinization of Salt.

Introduction

Thyroid diseases are one of the most important public health problems worldwide ranking second in endocrine diseases after diabetes mellitus. The micronutrients like iodine are a public health problem affecting all segments of the population [1]. 300 million people worldwide are affected by thyroid disorders [2]. Thyroid burden in India is estimated at 42 million [3]. Thyroid gland produces thyroxine (T4) and tri-iodothyronine, the two key hormones that regulate growth, metabolism, and development. These are under the control of anterior pituitary hormone thyrotropin (thyroid stimulating hormone TSH) which stimulates production of thyroid hormone. Thyroid hormone synthesis requires iodine a crucial mineral derived from sea food or iodized salt in the diet. The spectrum of thyroid function ranges from overactive hyper thyroidism to underactive hypothyroidism prevalence and pattern depends on age, sex, ethnic, geographical factors including iodine intake [4]. While abnormal function is more common in adults [5] the disorders are 8 times more common in women [6, 7].

Poverty and Thyroid Disorders

Poverty in India is contributing to the increase of thyroid disorders in several ways. According to studies, malnutrition, poor sanitation and lack of access to medical facilities in rural and impoverished areas of India is contributing to a higher prevalence of thyroid disorders.

Malnutrition, particularly iodine deficiency, is one of the major contributing factors to thyroid disorders in India [8]. The World Health Organization (WHO) states that iodine deficiency is the world's most common cause of preventable brain damage and intellectual disability. India is one of the countries with the highest prevalence of iodine deficiency, particularly in rural and poverty-stricken areas.

Poor sanitation in rural and impoverished areas of India is leading to exposure to harmful environmental pollutants and chemicals which have been linked to thyroid disorders [9]. The presence of heavy metals like cadmium, lead and mercury in the environment and food chain is affecting the thyroid function and leading to a higher prevalence of thyroid disorders.

Poverty in India is also contributing to the lack of access to medical facilities and diagnosis of thyroid disorders. Many rural and impoverished areas in India lack access to adequate medical facilities and diagnostic services. This results in a delayed diagnosis and treatment of thyroid disorders, leading to more severe complications and increased mortality rates [10]. In conclusion, poverty in India is contributing to the increase of thyroid disorders through malnutrition, poor sanitation, and lack of access to medical facilities.

Access to health care

In India, lack of access to healthcare can result in thyroid disorders going undiagnosed and untreated. This can occur due to various reasons such as, inadequate healthcare facilities and resources, particularly in rural areas, lack of awareness and understanding of the symptoms and causes of thyroid disorders, financial barriers that prevent individuals from seeking medical attention and treatment, limited availability of trained healthcare professionals and specialists in endocrine disorders. These factors can lead to individuals experiencing symptoms for long periods without receiving proper treatment, leading to the development and progression of thyroid disorders. It's important for individuals to have access to quality healthcare in order to diagnose and manage thyroid disorders effectively.

Without access to adequate medical facilities and trained healthcare professionals, individuals with thyroid conditions may not be able to receive the proper evaluation and treatment they need. This can result in their condition worsening over time and potentially leading to more serious health problems. Another factor is the lack of awareness about the symptoms and risk factors of thyroid disorders. In communities where access to health

education is limited, people may not understand the importance of seeking medical attention for symptoms that could be indicative of a thyroid problem.

Iodine intake - Recommended Intakes

Intake recommendations for iodine and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the Institute of Medicine of the National Academies [11]. DRI is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. These values, which vary by age and gender [11], include:

Recommended Dietary Allowance (RDA) - Average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals; often used to plan nutritionally adequate diets for individuals.

Adequate Intake (AI) - Intake at this level is assumed to ensure nutritional adequacy; established when evidence is insufficient to develop an RDA.

Estimated Average Requirement (EAR): Average daily level of intake estimated to meet the requirements of 50% of healthy individuals; usually used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them; can also be used to assess the nutrient intakes of individuals.

Tolerable Upper Intake Level (UL) - Maximum daily intake unlikely to cause adverse health effects.

Table - 1 lists the current RDAs for iodine [11]. For infants from birth to 12 months, the FNB established an AI for iodine that is equivalent to the mean intake of iodine in healthy, breastfed infants in the United States.

Table – 1: Recommended dietary allowances (RDAs) for iodine [11].

Recommended dietary allowances (RDAs) for iodine [11]				
Age	**Male**	**Female**	**Pregnancy**	**Lactation**
Birth to 6 months	110 mcg	110 mcg		
7 – 12 months	130 mcg	130 mcg		
1 – 3 years	90 mcg	90 mcg		
4 – 8 years	90 mcg	90 mcg		
9 – 13 years	120 mcg	120 mcg		
14 – 18 years	150 mcg	150 mcg	220 mcg	290 mcg
19 + years	150 mcg	150 mcg	220 mcg	290 mcg

The World Health Organization (WHO), United Nations Children's Fund (UNICEF), and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) recommend a slightly higher iodine intake for pregnant women of 250 mcg per day [12, 13].

Iodine is a trace element in the synthesis of thyroid hormones, and the thyroid gland secretes two metabolic hormones, thyroxine (T4) and triiodothyronine (T3), regulating metabolic rate, growth, and development [14, 15]. Disregulated thyroid hormones produced by the thyroid gland, can cause many disorders including hypothyroidism, subclinical hypothyroidism, hyperthyroidism, subclinical hyperthyroidism, and secondary hypothyroidism [15, 16].

Diseases of the thyroid gland are among the most common endocrinologic diseases. The size of the thyroid gland has been reported to increase with age, and the prevalence of goitre has reached 70% in populations with iodine deficiency [17, 18, 19]. Evident hypothyroidism is observed in approximately 1%–7% of the general population, where the rate for subclinical hypothyroidism is approximately 14%–18% [20].

The iodine intake ratio is the most important factor affecting thyroid diseases and prevalence in a population. Therefore, thyroid disease prevalence changes according to region and age [21]. The spectrum and the prevalence of thyroid disorders are known to be influenced by environmental factors, especially by iodine intake [4]. Indeed, iodine deficiency is regarded as the most common cause of thyroid disorders worldwide [21, 22, 23, 24].

The World Health Organization (WHO) has recommended that children 5 years of age or younger ingest 90 μg of iodine daily; children 6 to 12 years of age, 120 μg daily; adults, 150 μg daily; and pregnant or lactating women, 200 μg daily [25]. The prediction of iodine intake is difficult, if not impossible, because the amount of iodine in individual foods and in water can vary by a factor of 100 [26, 27]. The standard measure of iodine nutrition in a community or country is the median urinary iodine excretion, expressed in micro- grams per liter. The values correspond to 70 to 80 percent of the daily iodine intake, which often varies widely among people in the same community or country [28].

Iodine can come only from external sources mostly food, but also water. It is not widely distributed in nature; in the past, iodine deficiency was common among people on every continent. Many people are still deficient in iodine, despite major national and international efforts to increase iodine intake, primarily through the voluntary or mandatory iodination of salt.

Spectrum of disorders in iodine deficiency and iodine excess

Mild iodine deficiency results in learning disability, poor growth, and diffuse goiter in school-age children. These consequences of mild deficiency are easily understood the production of thyroid hormones is reduced, and the thyroid gland enlarges to compensate for the reduction. In adults, mild iodine deficiency is also associated with non-toxic nodular goiter and, less often, with toxic nodular goiter, because the constitutive (thyrotropin-independent) growth and functional potential of some clones of thyroid cells increases.

The spectrum of disorders of iodine excess also includes hypothyroidism and hyperthyroidism. Milligram or higher doses of iodine may cause hypothyroidism in people with damaged thyroid glands and normalization of thyroid secretion in those with hyperthyroidism. This anti-thyroid action of iodine is often short lived, owing to down regulation of iodine transport into the thyroid gland, but such down regulation does not occur in people with a damaged thyroid gland. Conversely, iodine in these quantities may induce hyperthyroidism in patients with a multinodular goiter or Graves' disease whose iodine intake is low, although it is unlikely to do so if the deficiency is not severe and if the increase in intake is relatively small.

A more important issue is whether some level of chronic iodine intake is harmful. Some classifications of iodine nutrition include categories of high or excessive iodine intake, because high levels of iodine intake have sometimes been associated with an increased risk of hyperthyroidism, hypothyroidism, or autoimmune thyroiditis. Indeed, fear of iodine induced thyroid dysfunction has at times delayed or limited the implementation of iodine supplementation in regions with iodine deficiency. The divergent effects of such supplementation on thyroid disorders may be related to underlying thyroid autonomy or genetic susceptibility to the disorders. The evidence for these increased risks is based largely on the results of cross sectional studies before and after iodine intake increased.

Iodine is an essential component of thyroid hormones; either low or high intake may lead to thyroid disease. More than adequate or excessive iodine intake may lead to hypothyroidism and autoimmune thyroiditis [29, 30].

Aim of the study

- To study the clinical spectrum of thyroid disorders in tertiary care hospital at Patancheru, Sangareddy, Telangana, India.

Materials and methods

It is a retrospective descriptive analysis carried out among the patients with thyroid disorders who attended the out-patient and in-patient in the Department of General Medicine, Maheshwara Medical College And Hospital, Isnapur, Patancheru, Telangana. Most of the patients belong to Patancheru Mandal of Sangareddy Dist. Telangana state, India.

Sample size: Total 57 Patients
Study duration: December 2017- January 2023

Study subjects: Patients attending out-patient and in-patient of the hospital with confirmed thyroid disorders.

Inclusion criteria

- Both sexes - Male and Female
- Age between 18-70 years
- All patients with thyroid disorders
- Those who have given the consent for study

Exclusion criteria

- Age <Below 18 years and >70 years
- Those without thyroid disorders
- Those who didn't give consent for the study

Diagnostic criteria

Following diagnostic criteria are followed for diagnosing various thyroid disorders as per **Table – 2**.

Table – 2: Diagnostic Criteria for Thyroid Diseases [29].

Thyroid Disease	**Diagnostic Criteria***
Overt hypothyroidism	Thyrotropin>4.8 mIU/liter, free T4 <10.3 pmol/liter
Subclinical hypothyroidism	Thyrotropin>4.8 mIU/liter, free T4 within the normal range
Autoimmune thyroiditis	TPOAb>100 IU/ml with overt or subclinical hypothyroidism
Hashimoto's thyroiditis With goiter	High serum autoantibody values TPOAb ≥50 IU/ml or TgAb ≥40 IU/ml
Atrophic thyroiditis Without goiter	
Overt hyperthyroidism	Thyrotropin<0.3 mIU/liter; free T4 >24.5 pmol/liter, free T3 >6.3 pmol/liter,or both
Subclinical hyperthyroidism	Thyrotropin<0.3 mIU/liter, free T3 and free T4 within the normal ranges
Graves' disease	Overt hyperthyroidism, a diffuse goiter or normal thyroid volume on B-mode ultrasonography, and TRAb>2 IU/liter or TPOAb>100 IU/ml
Goiter	Thyroid volume >19.4 ml (women) or >25.6 ml (men)
Diffuse Goiter without nodules	Diffuse swelling, no nodules, Thyroid volume >19.4 ml (women) or >25.6 ml (men)
Nodular Goiter with nodules	nodules >10 mm in diameter
Single nodule	Single nodule >5 mm in diameter, thyroid volume within the normal range
Multiple nodules	Nodules ≥2 Nodules >5 mm in diameter, thyroid volume within the normal range

*The reference range for free thyroxine (T4) is 10.3 to 24.5 pmol per liter; for free triiodothyronine (T3), 2.3 to 6.3 pmol per liter; for thyroid peroxidase antibody (TPOAb), 7 to 50 IU per milliliter; for thyroglobulin antibody (TgAb), 10 to 40 IU per milliliter; and for thyrotropin receptor antibody (TRAb), ≤2 IU per liter. To convert values for free T4 to nanograms per deciliter, multiply by 12.87 [29].

A total of 57 patients were included attending out-patient and in -patient of the hospital, having thyroid disorders. Data was collected from the medical records of the hospital and were analyzed based on the age, sex, different types of thyroid disorders and the medicines prescribed. Informed consent was also taken from them. Institutional Ethical Committee and Scientific Committee approval was taken.

Laboratory investigations: The serum samples were collected from the 57 subjects, Serum T3, T4 and TSH levels were estimated. TPO, Antithyroglobulin Ab and Anti ds DNA were also estimated. USG of thyroid, FNAC was also done in patients who consented.

Statistical analysis: The data were compiled in MS excel and analyzed. Data were described by percentages, ratios.

Results

Out of the 57 patients selected for the study, 54 (94.74%) patients were females followed by 3 (5.26%) males (**Table - 3**).

27 patients were in the age group between 18 and 30 years, followed by 12 patients between 31and 40 years, 13 patients in 41-50 years, 2 in 51-60 years, 3 between 61 and 70 years (**Table - 4**).

Two types of thyroid disorders were identified for the patients who visited from December 2017 to January 2023. The diagnosed thyroid disorders were as follows.

Out of 57 patients, 46 patients presented with hypothyroidism and 11 with hyperthyroidism.

With regards to gender and thyroid disorders, they are common in females. **Table - 3** shows the prevalence of thyroid disorder in different sex. Prevalence of thyroid disorders are different in different age group (**Table - 4**) shows the prevalence of thyroid disorders in different age group.

TPO and Anti Thyroglobulin Antibodies were done in five patients and were positive suggestive of Hashimatos Thyroiditis (**Table - 5**). One patient tested positive for Anti ds DNA, suggestive of SLE. Ultrasound findings were suggestive of Hashimatos Thyroiditis in 8 cases of hypothyroidism, and in hyperthyroid group, it was found Colloid Nodule in 1 and Diffuse Thyromegaly in 2 patients (**Table - 6**). FNAC was done in 4 patients (**Table - 7**). In one male hypothyroid patient it revealed Colloid goiter. FNAC in 3 female patients with hyperthyroidism revealed Graves disease, Colloid goiter, and Graves with Hashimotos thyroiditis. All the patients could not afford to get all the costly investigations done, because of financial constraints and fear for surgery (FNAC).

Discussion

Thyroid disorder is a neglected major public health issue and the most common non-communicable disease in developing countries [1, 31]. Thyroid disorder is the most common disease of the endocrine system which is increasing predominantly among females in the world [32].

Okpara, et al. reported a higher frequency of primary hypothyroidism (4.9%) and subclinical hypothyroidism (6.3%) [33]. This high frequency of hypothyroidism may be explained due to poor iodine nutrition, cultural beliefs, and barriers that delay the consumption or inadequate intake of these micronutrients including iodine [34].

Table - 3: Sex distribution.

Sex	No of patients
Female	54
Male	3

Table – 4: Age distribution.

Age distribution (years)	No of patients	Hypothyroidism		Hyperthyroidism	
		Male	Female		
18-30	27	02	20	00	05
31-40	12	00	09	00	03
41-50	13	00	11	00	02
51-60	02	02	00	00	00
61-70	03	01	01	00	01
Total	57	05	41	00	11

Table - 5: TPO and Anti Thyroglobulin Ab (F-Female; M- Male).

TPO & Anti Thyroglobulin Ab	Hypothyroidism	Hyperthyroidism
Not Done	43	09
Positive	03 F-2 ; M-1	02 F-2 ; M-0
Negative	00	00
Total	**46**	**11**

Table - 6: Ultrasound (F - Female; M - Male).

Ultra Sonogram of Thyroid	Hypothyroidism	Hyperthyroidism
USG Not Done	42	08
USG Test Done	04 F-3 ; M-1	03 F-3 ; M-0
Ultrasound findings	Suggestive of Hashimatos Thyroiditis	FEMALE: Colloid Nodule - 1 Diffuse Thyromegaly - 2

Table - 7: FNAC- Fine Niddle Aspiration Cytology (F- Femlae; M- Male)

FNAC	Hypothyroidism	Hyperthyroidism
FNAC not done	45	8
FNAC done	1 F-0 ; M -0	3 F-3 ; M-0
FNAC Findings	Male 1) Colloid goitre	Female 1)Graves disease 2) Colloid goitre 3)Graves with Hashimotos thyroiditis

Initiating programs such as the provision of enriching foods with iodine, prenatal Fe, and iodine vitamin supplements, raising public awareness of the disease either through mass media (TV, radio, and social media) or through posters in healthcare centers, and providing nutrition counseling and initiating plans of action to increase health literacy in the society are necessary for the prevention of thyroid disease in the early stages.

Diabetes mellitus is the most prevalent disorder in endocrinological diseases, while thyroid disorders were the second disease. Therefore, there is a link between thyroid dysfunction and diabetes which was documented in several studies that they are close diseases. Diabetes mellitus is associated with a higher prevalence of thyroid disease, and vice versa [35].

Studies in Nepal among thyroid co-morbid DM were shown in category three after the depression and hypertension [36].

Hypothyroidism may lead to many problems because of cardiac contractility arising from a reduction in cardiac output, increased peripheral vascular resistance, arrhythymia, delayed gastric emptying, increased susceptibility to a hypotensive effect of anesthetic agents and loosening of oropharyngeal tissues or difficult intubation due to a large tongue [37, 38, 39].

Measurements of the levels of TSH, fT3 and fT4 are among the most commonly used tests in the diagnosis of thyroid dysfunction. TSH level measurement is recommended as the most reliable test in all forms of hypothyroidism and hyperthyroidism in most guidelines [40].

Thyroid function tests increase costs at hospitals [41]. Some studies have indicated that TSH should be tested first for the follow up and the treatment of thyroid dysfunction; further tests are not required for those with normal TSH. In addition, testing for fT3 and fT4 in patients with abnormal TSH levels would decrease costs [42, 43].

Since iodine is essential for biosynthesis of thyroid hormones, insufficient dietary iodine and reduced supply of iodine to the thyroid gland will cause thyroid dyshormogenesis with attendant decreased synthesis, secretion and circulating levels of thyroid hormones [44, 45]. This primarily causes hypothyroidism which may be subclinical or overt. Often, iodine deficiency–induced hypothyroidism causes a compensatory increase in synthesis and secretion of TSH which in turn promotes growth and enlargement of thyroid tissue thereby causing goiter (euthyroid or hypothyroid goitre). Most iodine– deficiency goiters are associated with euthyroidism (euthyroid or simple goiters) at the initial stage. Without adequate iodine supplementation, simple goiters may progress to hypothyroid goiters with prevailing subclinicial or primary hypothyroidism [46]. This scenario is common among women of child-bearing age who are known to have increased demand for iodine and also higher prevalence of simple and hypothyroid goiters.

Our study showed that the highest frequency of TD occurred among women between the ages 16 and 40 years, who due to dietary iodine deficiency and increased iodine requirement during pregnancy and lactation, are prone to simple or hypothyroid goiters. Chronicity of iodine deficiency in patients with hypothyroid goiters causes compensatory increase in synthesis and secretion of TSH with increased stimulation of thyroid tissue growth, size, nodullarity, and function thereby causing nodular or multinodular goiters. Multinodular goitres are initially benign but may become toxic with time causing subclinical or overt hyperthyroidism [47].

In the present study thyroid dysfunction higher in females compared to males is consistent with various studies reported, 82.64% females and 17.35% males, male to female ratio 1:4.7 similar to 5:1 ratio in Oqbera A O, et al. [48] in south western region of Nigeria, Sidbe, et al. [49] in sub Saharan Africa mention 94.2% of female affected, Mahato R V, et al. [50], reported 83.27% females and 16.73% males, Karachi study [51] consisted of 85.5% females and 11.5% males and in Rosemary Iken, et al. [52] study 85.9% were female and 14.1% were male.

The most common type of thyroid disorder observed was total hypothyroidismm. These prevalence rates a consistent with several studies [53, 54]. Hypothyroidism is usually autoimmune in origin and is generally associated with iodine deficiency reported in endemic areas like Nepal [55] and thyroablative therapy. It tends to increase with age [56, 64] and is more common in women who are at risk of developing hypertension in pregnancy, increased risk of miscarriage, impaired mental performance in children born to untreated women [57]. By contrast hyperthyroidism is much less common. Graves' disease is most common cause and

affects younger adults while toxic multinodular goiter affects older adults [58]. Both hypothyroidism and subclinical hypothyroidism are known to be associated with serious consequences such as IHD [59], anxiety and depression disorders [60], proper guidelines are required for screening and management as utility of universal screening for hypothyroidism is non-uniform.

ATA (American Thyroid Association) recommends screening to begin at 35 years. age there after every 5 years [61], AACE(American Association of Clinical Endocrinologists) [62] recommends measurement in women trying to conceive or in 1st trimester, USPSTF [63] (United States Preventive Services Task Force) concluded that there is insufficient evidence to recommend universal screening.

Conclusion

High prevalence of hypothyroidism was observed in the present study, particularly in women across all age groups, and was the most common manifestation in the spectrum of thyroid dysfunction. Hypothyroidism can be insidious, associated with other conditions, hence should be screened in this setting and in whole population above 65yrs as most cases are diagnosed and managed within primary care setting.

In this study the number is less when compared to the huge population. Access to health care is not adequate to diagnose treat thyroid disorders. People are reluctant to give blood for investigations. And also they are reluctant to for FNAC or surgery. All sophisticated investigations are not available in any single laboratory. Patients need investigations repeatedly for follow up. Cost of investigations are prohibitive, it is beyond the capacity of patients.

All the investigations should be made available in many laboratories and the cost should be within the reach of common man. Awareness should be created in the population regarding thyroid disorders, and it should be stressed that once diagnosed they need to take treatment and need follow up for life.

It is my personal observation that the incidence of thyroid disorders is increased, as I have not seen so many thyroid disorders during 1980's and 1990's when compared to present scenario. The increased incidence coincides with the introduction of universal iodinization of salt in 1990's. It makes one to think that the possibility of increased incidence coincides with the introduction of universal iodinization of salt. Many scientific studies are needed to know the exact cause of spurt in thyroid disorders.

References

1. Mohamed A. Hassan-Kadle, Abdulkamil Abdullahi Adani, Hasan Huseyin Eker, et al. Spectrum and Prevalence of Thyroid Diseases at a Tertiary Referral Hospital in Mogadishu, Somalia: A Retrospective Study of 976 Cases. International Journal of Endocrinology, 2021; Article ID 7154250, 1-7.
2. Canaris GJ, Manowitz NR, Mayor G, et al. The Colorado thyroid disease prevalence study. Arch Intern Med., 2000; 160(4): 526-534.
3. Kochupillai N. Clinical endocrinology in India. Current Science, 2000; 79(8): 1061-1067.
4. Vanderpump MP, Tunbridge WM. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid, 2002; 12(10): 839-847.
5. Sawin CT, Castelli WP, Hershman JM, et al. The aging thyroid. Thyroid deficiency In Framingham study. Arch Intern Med., 1985; 145(8): 1386-1388.
6. Peter PAS. Epidemiology of thyroid dysfunction- hypothyroidism and hyperthyroidism. Thyroid International, 2009; 2: 1-16.
7. Sepuri M, Das Basumitra, Lakshmikantham A. Spectrum of thyroid dysfunction in North Coastal Andra

Pradesh. J. Evid. Based Med. Healthc., 2018; 5(28): 2091-2094.

8. Gupta S., Rajendran P., Rajan A. S. Iodine deficiency disorders (IDD) in India. Indian Journal of Medical Research, 2012; 135(5): 599-605.
9. Shukla R. K., Garg N., Garg V. K. Environmental pollutants and their impact on thyroid function: A review. Journal of Environmental Science, Toxicology and Food Technology, 2016; 10(1): 1-7.
10. Mishra S., Nema R. K., Singh S. B. Endemic goiter and iodine deficiency disorders in India: An overview. The Journal of Clinical Endocrinology & Metabolism, 2014; 99(7): 2399-2408.
11. Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (http://www.nap.edu/openbook.php?record_id=10026&page=1). (http://www.nap.edu/openbook.php?record_id=10026&page=1) Washington, DC: National Academy Press, 2001.
12. World Health Organization. United Nations Children's Fund & International Council for the Control of Iodine Deficiency Disorders. Assessment of iodine deficiency disorders and monitoring their elimination (http://whqlibdoc.who.int/publications/2007/9789241595827_eng.pdf). (http://whqlibdoc.who.int/publications/2007/9789241595827_eng.pdf) 3rd ed. Geneva, Switzerland: WHO, 2007.
13. WHO Secretariat, Andersson M, de Benoist B, Delange F, Zupan J. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutr., 2007 Dec; 10(12A): 1606-1611.
14. M. P. Vanderpump. The epidemiology of thyroid disease. British Medical Bulletin, 2011; 1(1): 99.
15. A. Agrawal, N. Rani, R. Maskey. Clinical profile of thyroid disorders–A retrospective study at BPKIHS. Journal of Diabetes and Endocrinology Association of Nepal, 2018; 2(2): 19–25.
16. A. S. Al Shahrani, A. El-Metwally, K. Al-Surimi, et al. The epidemiology of thyroid diseases in the Arab world: a systematic review. Journal of Public Health and Epidemiology, 2016; 8(2): 17–26.
17. Aykut Sarıtaş, Pelin Uzun Sarıtaş, Muhammed Murat Kurnaz, Abdullah Çelik. Spectrum and Prevalence of Thyroid Disorders in Patients Admitted to the Anesthesiology Outpatient Clinic for Surgery. Turk J Anaesth Reanim, 2015; 43: 240-5.
18. Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacha- rach P. The aging thyroid: thyroid deficiency in the Framing- ham study. Arch Intern Med., 1985; 145: 1386-8.
19. Cavaliere R, Antonangeli L, Vitti P, Pinchera A, Aghini-Lom- bardi F. The aging thyroid in a mild to moderate iodine deficient area of Italy. J Endocrinol Invest., 2002; 25: 66-8.
20. Tunbridge WMG, Evered D, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Wickham survey. Clin Endocrinol., 1977; 7: 481-93.
21. Aghini-Lombardi F, Antonageli L, Martino E, Vitti P, Mac- cherini D, Leoli F, et al. The spectrum of thyroid disorders in an iodine-deficient community: The Pescopagano survey. J Clin Endocrinol Metab., 1999; 84: 561-6.
22. Vanderpump MPJ, Tunbridge WMG. The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, eds. Werner and Ingbar's the thyroid. Philadelphia: Lippincott-Raven; 1996; 474–482.

23. Dunn JT, Pretell EA, Daza CH, Viteri FE. Towards the eradication of endemic goiter, cretinism and iodine deficiency. Pan American Health Organization. Washington: WHO; Scientific publication, 1986; 502: 215–370.
24. Delange F. The disorders induced by iodine deficiency. Thyroid, 1994; 4: 107–128.
25. WHO global database on iodine deficiency. Geneva: World Health Organization. (Accessed June 8, 2006, at http://www3. who.int/whosis/micronutrient.)
26. Pearce EN, Pino S, He X, Bazrafshan HR, Lee SL, Braverman LE. Sources of dietary iodine: bread, cows' milk, and infant formula in the Boston area. J Clin Endocrinol Metab., 2004; 89: 3421-4.
27. Pedersen KM, Laurberg P, Nøhr S, Jørgensen A, Andersen S. Iodine in drinking water varies by more than 100-fold in Denmark: importance for iodine content of infant formulas. Eur J Endocrinol., 1999; 140: 400-3.
28. Robert D. Utiger. Iodine Nutrition — More Is Better. N Engl J Med., 354; 26: 2819-21.
29. Weiping Teng, Zhongyan Shan, Xiaochun Teng, et al. Effect of Iodine Intake on Thyroid Diseases in China. N Engl J Med., 2006; 354: 2783-93.
30. Robert D. Utiger. Iodine Nutrition — More Is Better. The New England Journal of Medicine, 2006, 354; 26; 2819-21.
31. J. Fualal, J. Ehrenkranz. Access, availability, and infra- structure deficiency: the current management of thyroid disease in the developing world. Reviews in Endocrine & Metabolic Disorders, 2016; 17(4): 583–589.
32. J. Antony, T. Celine, M. Chacko. Spectrum of thyroid disorders: a retrospective study at a medical college hospital. Thyroid Research and Practice, 2014; 11(2): 55–59.
33. H. C. Okpara, A. B. Ene, E. O. Enang, T. M. Aluka. Spectrum of thyroid dysfunction among patients evaluated by thyroid function tests at a tertiary clinical laboratory in Calabar, Nigeria. Annals of Medical and Health Sciences Research, 2017; 7: 411–417.
34. "Consensus reached at the FAO/WHO international conference on nutrition in 1992," 2021, https://extranet.who.int/ nutrition/gina/sites/default/filesstore/SO M_MN%20Strategy %20-%202014-2016.pdf.
35. B. Biondi, G. J. Kahaly, R. P. Robertson. Thyroid dysfunction and diabetes mellitus: two closely associated disorders. Endocrine Reviews, 2019; 40(3): 789–824.
36. P. Gupta, P. K. Agrawal, B. Gauchan. Prevalence of thyroid disorder in A primary care district hospital of Nepal. Journal of the Nepal Medical Association, 2019; 57(216): 109–112.
37. Farling PA. Thyroid disease. Br J Anaesth., 2000; 85: 15-28.
38. Tulunay M, Cuhruk H. Klinik Anesteziyoloji Eds: Morgan GE, Mikhail MS, Murray MJ 4. Ed: 2008, p. 802-17.
39. Turan IO, Yurtlu BS. Tiroid ve paratiroid hastalıkları ve anes- tezi. Turkiye Klinikleri J Anest Reanim, 2010; 3: 1.
40. Tekçe B, Dikbaş O, Tekçe H, Tosun M. Evaluation of the re- quests for thyroid function test according algorithms and cost effectivity. Abant Med J, 2013; 2: 114-8.
41. Kumar VV, Kaimar P. Subclinical hypothyroidism: A cause for delayed recovery from anaesthesia? Indian J Anaesth., 2011; 55: 433-4.
42. John R, Henley R, Lloyd G, Elder GH. Evaluation of a new strategy for detection of thyroid dysfunction in the routine lab- oratory. Clin Chem., 1988; 34: 1110-4.
43. Klee GG, Hay ID. Assessment of sensitive thyrotropin assays for an

expanded role in thyroid function testing: proposed cri- teria for analytic performance and clinical utility. J Clin Endo- crinol Metab., 1987; 64: 461-71.
44. Vanderpas J. Nutritional epidemiology and thyroid hormone metabolism. Ann Rev Nutr., 2006; 26: 293-322.
45. Kirsten D. The thyroid gland: Physiology and pathophysiology. Neonatal Netw., 2000; 8: 11-26.
46. Triggiani V, Tafaro E, Giagulli VA, Sabba C, Resta F, Licchelli B, et al. Role of iodine, selenium and other micronutrients in thyroid function and disorders. Endocr Metab Immune Disorder Drug Targets, 2009; 18: 277-294.
47. Krohn K, Fuhrer D, Bayer Y, Eszlinger M, Brauer V, Neumann S. et al. Molecular pathogenesis of euthyroid and toxic multinodular goitre. Endocr Rev., 2005; 26: 504-524.
48. Ogbera AO, Fasanmade O, Adediran O. Pattern of thyroid disorders in the southwestern region of Nigeria. Ethn Dis. 2007; 17(2): 327-330.
49. Sidibe eL H. Thyroid diseases in Sub-Saharan Africa. Sante, 2007; 17(1): 33-39.
50. Mahato RV, Nepal AK, Gelal B, et al. Spectrum of thyroid dysfunction in patients visiting Kantipur hospital, Kathmandu, Nepal. Mymensingh Med J., 2013; 22(1): 164-169.
51. Maqsood A, Shakir MM, Shahid R, et al. Spectrum of thyroid gland disorders in Karachi –DDRRL experience. Medical Forum Monthly, 2012; 23(4): 12-15.
52. Ikem R, Adebayo J, Soyoye D, et al. Spectrum of thyroid disorders in Obafemi Awolowo university teaching hospital complex. Endocrine, 2010; 21: 366- 367.
53. Tunbridge WM, Evered DC, Hall R, et al. The spectrum of thyroid disease in a community: the Wickham survey. Clin Endocrinol (Oxf), 1977; 7(6): 481-493.
54. Aminorroaya A, Janghorbani M, Amini M, et al. The prevalence of thyroid dysfunction in an iodine sufficient area in Iran. Arch Iran Med., 2009; 12(3): 262- 270.
55. Gelal V, Aryal M, Das BK, et al. Assessment of iodine nutrition status among school age children of Nepal by urinary iodine assay. South Asian J Trop Med Public Health, 2009; 40(3): 538-543.
56. Niafar M, Aliasgharzadeh A, Bahrami A, et al. Prevalence of thyroid dysfunction in the elderly women of Iran. Endocrine Abstracts, 2009; 20: 137.
57. Rodondi N, Aujesky D, Vittinghoff E, et al. Subclinical hypothyroidism and the risk of coronary heart disease: a meta-analysis. Am J Med., 2006; 119(7): 541-551.
58. Wu Patricia. Diabetes and thyroid disease. Clinical Diabetes, 2008; 18: 111-118.
59. Biondi B, Palmieri EA, Lombardi G, et al. Subclinical hypothyroidism and cardiac function. Thyroid, 2002; 12(6): 505-510.
60. Almeida C, Brasil MA, Costa AJ, et al. Subclinical hypothyroidism: psychiatric disorders and symptom. Rev Bras Psiquiatr., 2007; 29(2): 157-159.
61. Ladenson PW, Singer PA, Ain KB, et al. American thyroid association guidelines for detection of thyroid dysfunction. Arch Intern Med., 2000; 160(11): 1573-1575.
62. Baskin HJ, Cobin RH, Duick DS, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocrine Prac., 2002; 8(6): 457-469.
63. Surks MI, Oritz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA, 2004; 291(2): 228-238.

64. Madhuri Sepuri, Basumitra Das, Adapaka Lakshmikantham; Spectrum of thyroid dysfunction in north coastal Andhra Pradesh. J. Evid. Based Med. Healthc, 2018; 28(5): 2349-2570.