

# Prevalence of Hyperthyroidism among Students Age 6 to 14 Years in Dessie City, Northeast Ethiopia

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## ABSTRACT:

**Background:** Hyperthyroidism is a pathologic syndrome in which excess thyroid hormone is synthesized and secreted by the thyroid gland, resulting in the hyper metabolic state of thyrotoxicosis. Therefore, this study aimed to determine hyperthyroidism among students aged 6 to 14 years in the city of Dessie, Amhara region, Ethiopia, from April to June 2019.

**Methods:** An institution-based cross-sectional study design was used, and a systematic random sampling technique was applied to select study participants. Socio-demographic characteristics were assessed using a pretested questionnaire, and Blood samples were collected to measure serum thyroid stimulating hormone), free tetra iodothyronine levels, and tri-iodothyronine levels determined via chemiluminescence immunoassays run on an automated Maglumi 800 Hormone Analyzer. Data were cleaned, coded, and entered Epi Info Data version 3.1 and then exported to SPSS version 21 software for statistical testing.

**Results:** A total of 564 school-aged children were included in the study. Of 564 students, only 22 (3.9%) had hyperthyroidism, and 542 did not have hypothyroidism (96.1%), The most common age group was 6–8 years with hyperthyroidism (15.2%), and the female sex was more prevalent (54.5%) than male (45.5%).

**Conclusions and Recommendations:** In this study, the prevalence of hyperthyroidism among students aged 6 to 14 years was 3.9. It was more prevalent in female students in the age group of 6–8 years old. In such cases, more determinant explanatory studies are advised.

**Keywords:** screening, hyperthyroidism, students, Amhara region, Dessie, Ethiopia

## የጥናቱ ረቂቅ

**የጥናቱ ዳራ:** ሃይፐርታይሮዲዝም ከመጠን በላይ የሆነ የታይሮይድ ሆርሞን በታይሮይድ ዕጢ አማካኝነት መመረትና መመንጨት ምክንያት የሚመጣ የበሽታ ምልክት ነው። ይህም ከፍተኛ የሆነ የታይሮቶክሲኮሲስ ሁኔታ ያስከትላል። ስለሆነም የዚህ ጥናት አላማ የሃይፐርታይሮዲዝምን ስርጭት በደሴ ከተማ ከ6 እስከ 14 አመት እድሜ ክልል ውስጥ ባለ-ተማሪዎች ላይ ለማወቅ ነው።

**የጥናቱ ስልት/ዘዴ:** በድምሩ 564 ከ6-14 ዓመት እድሜ ክልል ያሉ ተማሪዎችን በጥናቱ ተካተዋል። በተቋም ላይ የተመሰረተ የጥናት ንድፍ ሃሰብ ጥቅም ላይ ውሏል። የጥናት ተሳታፊዎችን ለመምረጥ ስልታዊ ናሙና አዎንታዊ ዘዴ ተተግብሯል። ስነ-ሕዝብ ባህሪያት መጠይቅ ለማዘጋጀት ቀድሞ ከተገመገመ ደረጃውን በጠበቀ መመሪያ ላይ የተወሰደ ነው። የደም ናሙናዎች የተሰበሰቡት የሴሪም ታይሮይድ አኑቃቂ ሆርሞንን፣ ነጻ ቲትራ-አዮዶታይሮኒን ደረጃ መጠንን እና ቲትራ-አዮዶታይሮኒን ደረጃን ለመወሰን አውቶማቲክ ማገላጫ 800 ሆርሞን ተንታኝ ማሽን በመጠቀም የኬሚሊሚኒዘሴንስ ኢሙኖአሴይ ምርመራ ተሰርቷል። የተሰበሰበው መረጃ ወደ SPSS 21

ሶፍትዌር መረጃውን በመወሰድ እንዲተነተን ተደርጓል።

**የጥናቱ ውጤት:** በድምሩ 564 እድሜያቸው ለትምህርት የደረሱ ህጻናት በጥናቱ ውስጥ ተካተዋል። ከ 564 ተማሪዎች ውስጥ 22 (3.9%) ብቻ የሃይፐርታይሮዲዝም ስርጭት ሲኖርባቸው 542 ሃይፖታይሮዲዝም (96.1%) የላቸውም። ከፍተኛ ሃይፐርታይሮዲዝም ስርጭት (15.2%) የነበራቸው የዕድሜ ክልል ከ6-8 አመት ሲሆኑ የሴት ተማሪዎች ሃይፐርታይሮዲዝም ስርጭት (54.5%) ከወንድ ተማሪዎች ሃይፐርታይሮዲዝም ስርጭት (45.5%) የበለጠ ነበር።

**ማጠቃለያና ምክረ ሃሳብ:** በዚህ ጥናት ከ6 እስከ 14 አመት የሆናቸው ተማሪዎች የሃይፐርታይሮዲዝም ስርጭት 3.9 በመቶ ነበር። በዚህ ጥናት ውስጥ የሃይፐርታይሮዲዝም ስርጭት በዎታ ንዕስር ስንመለከት፣ ከ6-8 አመት ባለው የዕድሜ ክልል ውስጥ ባለ ሴት ተማሪዎች ላይ ከፍ ያለ ነው። በእንደዚህ ዓይነት ሁኔታዎች ውስጥ ያለውን ችግር ለመፍታት ለወደፊቱ ብዙ የጥናት ተሳታፊዎችን ያካተተ የምርምር ጥናት እንዲሰራ ይመከራል።

**የጥናቱ ቁልፍ ቃላት፡** ልዩታ፣ ሃይፐርታይሮይዲዝም  
፣ በትምህርት ላይ ያሉ ልጆች ፣ አማራ ክልል ፣ ደሴ  
፣ ኢትዮጵያ

## BACKGROUND

The thyroid is a ductless endocrine gland that is found directly below the larynx on either side of the trachea and anterior to it. Thyroid Stimulating Hormone (TSH), Free Tri-iodothyronine (FT3), and Free Tetra-iodothyronine (FT4) are the main hormones generated by the thyroid gland in healthy people.<sup>1</sup> A pathological condition known as hyperthyroidism occurs when the thyroid gland produces and secretes an excessive amount of thyroid hormone.<sup>2</sup> It is a rare but potentially serious disorder especially in childhood that, if uncontrolled, can lead to a wide range of complications, including growth and development disorder.<sup>3</sup>

Clinical manifestation varies depending on several factors, such as the patient's age and sex, comorbidities, duration of the disease, and the causative factor. Older patients present with fewer and less pronounced symptoms than younger patients but are more likely to develop cardiovascular complications.<sup>4</sup> Atrial fibrillation, congestive heart failure, osteoporosis, and neuropsychiatric disorders are consequences of untreated hyperthyroidism.<sup>5</sup>

Students aged 6 to 14 years are the preferred group for thyroid function studies because of their high vulnerability, ease of access, and the high effectiveness of the treatment in this population.<sup>6</sup> Symptoms of hyperthyroidism affect the functional status and quality of life. A risk factor for developing these complications is asymptomatic thyroid dysfunction, which can be diagnosed by thyroid function tests before symptoms and complications appear. The purpose of screening is to identify and treat patients with subclinical thyroid dysfunction before they develop complications of hyperthyroidism.<sup>7</sup> Serum TSH is measured first because it has the highest sensitivity and specificity in the diagnosis of thyroid disorders.<sup>8</sup>

If low TSH is detected, measure serum-free or free T4 index and free or total T3 concentration to distinguish between normal circulating hormones and overt hyperthyroidism (suppressed TSH is  $< 0.1$  mIU per mL) or Elevated serum FT3 and FT4), including subclinical hyperthyroidism (mean suppressed TSH of  $0.2$  mIU/L and normal free T4) form. It also identifies disorders with increased thyroid hormone concentrations and normal or only slightly raised TSH concentrations.<sup>9</sup>

Globally, hyperthyroidism is a widespread disorder with many recorded cases due to a variety of factors such as dietary iodine consumption, ethnic origin, and population structure.<sup>10</sup> It is the most common cause in iodine-deficient areas, and while it increases with age, it remains quite common in women of reproductive age.<sup>11</sup> But to the best of our knowledge, the presentation was unable to find any study describing the overall prevalence of hyperthyroidism in the students aged 6–14 years. So far, there is a scarcity of data in the study area indicating hyperthyroidism screening using laboratory methods. Therefore, this study attempted to screen an asymptomatic case of hyperthyroidism, which has an important public health implication to give baseline data for clinicians, health sector administrators, concerned bodies, and researchers.

## METHODS

### Study design and period

A school-based cross-sectional study was employed to determine the prevalence of hyperthyroidism among student aged 6 to 14 years in Dessie city, Amhara region, Ethiopia from April 01/2019 to June 30/ 2019.

### Study area

The study was conducted in Dessie city administration in Amhara regional state, Northeast Ethiopia which has 18 urban and 8 rural districts. Based on the 2007 Central Statistical Agency of Ethiopia, this city has an estimated total population of 151,094 of whom 72,891 are men and 78,203 are women.<sup>12</sup> Dessie city is located at an altitude of 2,470 meters above sea level and has a subtropical highland climate. The city has 45 governmental and 12 private schools. In 2018, an estimated 38,068 (18,900 males and 19,168 females) students aged 6 to 14 were found in the city.

### Source and study population

The source populations for this study were students aged 6-14 years residing in Dessie city. Randomly selected students aged 6-14 years who fulfils the inclusion criteria were the study population.

### Sample size determination

The sample size was calculated using Epi-Info version 7 and the single population proportion formula with the following assumptions in mind: a 5% margin of error, a 95% confidence level, and a 50% prevalence of hyperthyroidism since there are no studies showing the prevalence of hyperthyroidism among students

aged 6–14 years in Ethiopia. The final sample size was 634 after adding a 10% non-response rate and 1.5 design effect.

### Sampling technique

A multistage sampling technique was used. Firstly, we randomly choose 12 schools out of a total of 57, and then the lists of all eligible students aged 6–14 years were taken from the respective schools for the sampling frame. Secondly, proportional size allocation was made to determine the required sample size from each school, and a systematic random sampling technique was applied to select the required number of students from each school. Students who were absent on the date of data collection were substituted by the next student in the sampling frame.

### Data collection procedure

Semi-structured questionnaire translated into Amharic was administered. Data was collected by professional data collectors from the mother or care giver of the child who came to school.

Venous blood samples (3-5 ml) were collected from each student between 9:30 and 10:00 AM using a metal-free safety vacutainer tube or 5 cc syringe, then reversed to the K2EDTA tube immediately. The blood samples were left standing for one hour; sera were separated by centrifugation at 2500 revolutions per minute and preserved at -20 °C until analysis. Blood samples were collected to measure serum TSH, FT4, and FT3 using chemiluminescence immunoassays run on an automated Maglumi 800 Hormone Analyzer in the Amhara Public Health Institute Dessie branch clinical chemistry department.

### Data quality control

To assure the quality of the data in the study, data collectors and supervisors were trained, and regular supervision and follow-up were made on a daily basis. The English version of the questionnaire is translated into Amharic and back-translated to English by translators who are blind to the original questionnaire. To assure the quality of the data, high emphasis is given to designing a data collection instrument for its simplicity, and a pre-test is conducted on 5% of the total sample size of the respondents from Kombolcha town students aged 6-14, followed by modifications made before the data collection. General safety

procedures, standard operating procedures were followed during diagnosis, and to control the quality of the automated Maglumi 800 Hormone Analyzer was checked by running internal quality control.

### Data analysis

After a thorough check-up for completeness, free from any error, the data was coded, cleaned, and entered into Epi-Info version 7.0 and exported to SPSS version 21 for analysis. Then descriptive frequencies were used for checking outliers and cleaning the data. The frequency distribution of dependent and independent variables was worked out. Bivariate and multivariable logistic regression was used to examine the factors. The degree of association was assessed by using an Odds ratio with a 95% confidence level. A P-value of 0.05 was considered statistically significant.

### Definition of terms

**Subclinical hyperthyroidism:** suppressed TSH (mean suppressed TSH of 0.2 mIU/L) with normal FT3 and FT4.<sup>13</sup>

**Hyperthyroidism:** Elevated serum FT3 and FT4 with suppressed serum TSH (suppressed TSH is < 0.1 mIU per L).<sup>13</sup>

**Euthyroid:** is the term given to describe a state of normal thyroid function in the body or Isolated elevation of FT4 in the presence of TSH, FT3 within normal reference limits, or Low FT3 in the presence of normal FT4 values (total FT3 and in the reference population regardless of age ranged from 2.4–8.8 (mean  $4.6 \pm 0.9$ ) pmol/L and 10.1–24.8 (mean  $15.40 \pm 2.0$ ) pmol/L, respectively) and TSH (normal TSH levels (0.4–4.1 mIU/L) (13).<sup>14</sup>

## RESULTS

### Socio-demographic characteristics

A total of 564 students aged 6 to 14 years were included in the study, with a response rate of 88.9%. The majority of the students were female, 321 (56.9%), with a median age of 12 years (SD = 2.1 years). More than half of the participants were between the ages of 12 and 14, and 60.8% had less than five family sizes. The majority of the students' mothers were married (80%) and housewives (44%). Thirty-eight (6.7%) of the participants had a family history of goiter (Table 1)

Table 1. Socio-demographic characteristics of students aged 6 to 14 years and their parents in Dessie city, Northeast Ethiopia (N=564), 2019.

Characteristics		Frequency	Percent
Sex of children	Male	243	43.1
	Female	321	56.9
Age of children	6-8 years	66	11.7
	9-11 years	198	35.1

Characteristics		Frequency	Percent
Marital status of mothers/caregivers	12-14 years	300	53.2
	Married	451	80.0
	Single	28	5.0
	Divorced	64	11.3
	Widowed	21	3.7
Educational status of mother/caregiver	Unable to read write	138	24.5
	Able to read write	158	28.0
	Primary education	200	35.5
	Secondary education and above	68	12.1
Occupation of mother	House wife	248	44.0
	Civil servant	90	16.0
	Merchant	54	9.6
	Others	172	30.5
	Family size	<5	343
	>= 5	221	39.2
Family history of goiter	Yes	38	6.7
	No	526	93.3

### Prevalence of Hyperthyroidism

In our finding the prevalence of hyperthyroidism was 3.9% (22/564) and 96.1% (542/564) students had normal thyroid levels. As shown in table 2: below, a comparable proportion of hyperthyroidism is observed among males 1.8% (10/564) and females 2.1%

(12/564) but study participants within the age group 6 to 8 years 1.8% (10/564) had a slightly higher proportion of hyperthyroidism. Regarding the family history of goiter, no students were found to have hyperthyroidism with a family history of goiter (Table 2)

Table 2. Proportion of Hyperthyroidism by child age, gender and family history of goiter among students aged 6 to 14 in Dessie city, Northeast Ethiopia (N=564), 2019.

Characteristics		Hyperthyroidism		
		No	Yes	Total
Sex	Male	233(41.3 %)	10(1.8%)	243(43.1%)
	Female	309(54.8%)	12(2.1%)	321(56.9%)
Age	6-8 years	56(9.9%)	10(1.8%)	66(11.7%)
	9-11 years	192(34%)	6(1.1%)	198(35.1%)
	12-14 years	294(52.1%)	6(1.1%)	300(53.2%)
Family history of goiter	Yes	38(6.7%)	0(0%)	38(6.7%)
	No	504(89.4%)	22(3.9%)	526(93.3%)
Total		542 (96.1)	22 (3.9)	

### Hyperthyroidism and associated factors

In the first bivariate regression model, the age of the child, educational status of the mother, marital status of mothers/caregivers, and occupation of the mother were identified as factors associated with hyperthyroidism with a p-value less than 20%. However, as depicted in Table 3, in a multivariable logistic regression analysis, the age of the child and the educational status of the mother were the only independent variables significantly associated with hyperthyroidism.

The results revealed that as increased age of the child was negatively associated with hyperthyroidism. As a result, the age of the child between 12-14 years was 0.86 times less likely to have hyperthyroidism than those children aged between 9-11 years (AOR = 0.813; 95% CI: (0.059-0.588)). The odds of hyperthyroidism were 0.803 times less likely among mothers having primary education than mothers unable to read and write (AOR=0.803; 95% CI: (0.039-0.985)) (Table 3).

Table 3. Binary and Multivariable logistic regression analysis of hyperthyroidism among students aged 6 to 14 years, Dessie, Amhara region, Ethiopia, 2019.

Variable name	Categories	Hyperthyroidism		COR(95%CI)	P-value	AOR(95%CI)	P-value
		Yes	No				
Age in years	6-8 years	10	56	1		1	
	9-11 years	6	192	0.175(0.061-0.503)		0.187 (0.059-0.588)	0.004
	12-14 years	6	294	0.114(0.040-0.327)		0.140 (0.044-0.448)	0.001
Educational status of the	Unable to read write	10	128	1		1	
	Able to read write	6	152	0.505(0.179-1.428)		0.672 (0.218-2.071)	0.488

Variable name	Categories	Hyperthyroidism		COR(95%CI)	P-value	AOR(95%CI)	P-value
		Yes	No				
mother	Primary education	2	198	0.129(0.028-0.60)		0.197 (0.039-0.985)	0.048
	Secondary and above	4	64	0.80(0.242-2.65)		(0.2.342 (.577-9.514)	0.234
Marital status of mothers/care givers	Married	12	439	1		1	
	Single	2	26	2.8(0.598-13.237)		1.283(.233-7.065)	0.774
	Divorced	8	56	5.3(2.048-13.337)		2.388(0.822-6.939)	0.110
	Widowed	0	21	0.000		0.000(0.000-0.000)	0.998
Occupation of mother	House wife	6	242	1		1	
	Civil servant	1	89	0.280(0.105-0.743)	0.011	0.251(0.027-2.345)	0.226
	Merchant	1	53	0.127(0.016-0.980)	0.048	0.589(0.065-5.298)	0.636
	Others	14	158	0.213(0.027-1.658)	0.140	2.369 (0.811-6.922)	0.115

## DISCUSSION

The prevalence and pattern of hyperthyroidism are difficult to compare across countries due to differences in diagnostic thresholds, assay sensitivities, population selection, fluxes in iodine nutrition, and population dynamics.<sup>15</sup> However, in this study, only 3.9% of students had hyperthyroidism, compared to 96.1% who did not. A study conducted in Ethiopia showed that TSH levels increased by 18.92%,<sup>16</sup> which is difficult to compare because show only TSH level only. In Khartoum State, Sudan similar method but the age range <25 revealed that 23.3% of them were hyperthyroidism.<sup>17</sup> About 1 out of 100 Americans ages 12 years and older have hyperthyroidism.<sup>18</sup> Globally many cases of hyperthyroidism remain undiagnosed in the community unless routine testing is undertaken.<sup>19</sup>

The proportion of hyperthyroidism was comparable across females 12(2.1%) and males 10(1.8%) and did not have a significant association between it. Related increase in thyroid size was similar in males and in females up to menarche, but significantly larger in girls after menarche.<sup>20</sup> Another study showed that the significant finding in males (Chi-square value=85.487, P<0.01) and in females (Chi-square value=60.820, P<0.01). However, the fact that there were only a very small number of participants in the age subgroup of < 25 years.<sup>21</sup>

Increase in age represents an important factor to define the aggressiveness of thyroid carcinomas. Both follicular and anaplastic types of thyroid cancer are more frequently found in elderly subjects.<sup>22</sup> Study shows that hyperthyroidism in the elderly is a serious clinical condition that is associated with significant morbidity and excess mortality.<sup>23</sup> In this study age, 6-8 years show higher prevalence than the above age groups. These findings suggest that physiological thyroid growth during puberty is mainly influenced by growth factors involved in somatic development and further modulated by sex steroid secretion profiles.<sup>20</sup>

Study shows that a family history of goiter variously has marked associations with hyperthyroidism but in this study having a family history of goiter has no associations and no hyperthyroidism at all with a family history of goiter.<sup>24</sup> The limitation of this study was that it was only conducted in one city, not in other high- and lowland areas with varied iodine levels.

Conclusion and recommendation: Students in this study have a lower prevalence of hyperthyroidism (3.9%) and no hyperthyroid disorder (96.1%). In our finding, a comparable proportion of hyperthyroidism was observed among females (12.1%) and males (10.8%), but study participants within the age group 6 to 8 years (10.8%) had a slightly higher proportion of hyperthyroidism.

Hyperthyroidism was negatively associated with the student's age and the educational status of the mother. Even though, according to our findings, we suggest that hyperthyroidism shows a lower prevalence in the study area, we recommend studies like mass screening, and cohort study design to know the prevalence of asymptomatic cases, in the different study areas and study populations to give appropriate intervention.

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## ABBREVIATIONS

DHS: Demographic and Health Survey Report, FT4: Free Fraction of Thyroxin, free T3 (FT3; tri-iodothyronine), SAC: School-Age Children (6–12

years), TSH: thyroid-stimulating hormone WHO: World Health Organization.

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

To obtain the consent and cooperation of relevant organizations, we obtained ethical approval from the Amhara Public Health Institute Ethical Review Board. Additionally, confidentiality was maintained by maintaining privacy at all levels of the study. The Declaration of Helsinki was followed when conducting the study.

### AVAILABILITY OF DATA AND MATERIALS

All the datasets analyzed during the current study are available from the corresponding author upon reasonable request.

### COMPETING INTERESTS

The authors declare no competing interests.

### REFERENCES

- <sup>1</sup>Thakur S, Agrawal M, Ghimire N, Bedajit RK, Roy P. Pattern of thyroid disorders in ENT OPD of Nobel Medical College in Eastern Nepal. *Journal of Diabetes and Endocrinology Association of Nepal*. 2019;3:26-31.
- <sup>2</sup>De Leo S, Lee SY, Braverman LE. Hyperthyroidism. *Lancet* (London, England). 2016;388(10047):906-918.
- <sup>3</sup>Srinivasan S, Misra M. Hyperthyroidism in children. *Pediatrics in review*. 2015;36(6):239-248.
- <sup>4</sup>Goichot B, Caron P, Landron F, Bouée S. Clinical presentation of hyperthyroidism in a large representative sample of outpatients in France: relationships with age, aetiology and hormonal parameters. *Clin Endocrinol* (Oxf). 2016;84(3):445-451.
- <sup>5</sup>Reid JR, Wheeler SF. Hyperthyroidism: diagnosis and treatment. *American family physician*. 2005;72(4):623-630.
- <sup>6</sup>Organization WH. Urinary iodine concentrations for determining iodine status in populations. *World Health Organizations*;2013.
- <sup>7</sup>Eber O, Langsteger W, Florian W, et al. [Evaluating thyroid gland function in patients with protein anomalies]. *Acta Med Austriaca*. 1991;18(1):11-19.
- <sup>8</sup>de los Santos ET, Starich GH, Mazzaferri EL. Sensitivity, specificity, and cost-effectiveness of the sensitive thyrotropin assay in the diagnosis of thyroid disease in ambulatory patients. *Arch Intern Med*. 1989;149(3):526-532.

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### AUTHORS' CONTRIBUTIONS

BS conceived the study, carried out the overall design, analyzed, and interpreted the data. MM, TA and SL drafted the manuscript and revised it critically for important intellectual content. MS assisted with the development of the questionnaire and drafted the manuscript. All authors read and approved the final manuscript.

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- <sup>9</sup>Vaidya B, Pearce SHS. Diagnosis and management of thyrotoxicosis. *BMJ : British Medical Journal*. 2014;349:g5128.
- <sup>10</sup>Taylor PN, Albrecht D, Scholz A, et al. Global epidemiology of hyperthyroidism and hypothyroidism. *Nature Reviews Endocrinology*. 2018;14(5):301-316.
- <sup>11</sup>Abraham-Nordling M, Byström K, Törning O, et al. Incidence of hyperthyroidism in Sweden. *Eur J Endocrinol*. 2011;165(6):899-905.
- <sup>12</sup>Zekaria S. Summary and statistical report of the 2007 population and housing census, United Nations Population Fund (UNFPA); 2008.
- <sup>13</sup>Biondi B, Cooper DS. Subclinical hyperthyroidism. *New England Journal of Medicine*. 2018;378(25):2411-2419.
- <sup>14</sup>Chopra IJ. Euthyroid sick syndrome: is it a misnomer? *The Journal of Clinical Endocrinology & Metabolism*. 1997;82(2):329-334.
- <sup>15</sup>Keestra S, Höggqvist Tabor V, Alvergne A. Reinterpreting patterns of variation in human thyroid function: An evolutionary ecology perspective. *Evolution, Medicine, and Public Health*. 2021;9(1):93-112.
- <sup>16</sup>Kibatu G, Nibret E, Gedefaw M. The status of iodine nutrition and iodine deficiency disorders among school children in Metekel zone, Northwest Ethiopia. *Ethiopian journal of health sciences*. 2014;24(2):109-116.
- <sup>17</sup>Medani K. Prevalence of Thyroid Disorders and Reference Range of Thyroid Hormones in

- Khartoum State, Sudan. *Journal of Research in Medical and Dental Science*. 2020;8:158-161.
- <sup>18</sup>De Leo S, Lee SY, Braverman LE. Hyperthyroidism. *The Lancet*. 2016;388(10047):906-918.
- <sup>19</sup>Braverman LE, Cooper D. *Werner & Ingbar's the thyroid: a fundamental and clinical text*. Lippincott Williams & Wilkins; 2012.
- <sup>20</sup>Fleury Y, Van Melle G, Woringer V, Gaillard RC, Portmann L. Sex-dependent variations and timing of thyroid growth during puberty. *The Journal of Clinical Endocrinology & Metabolism*. 2001;86(2):750-754.
- <sup>21</sup>Meng Z, Liu M, Zhang Q, et al. Gender and Age Impacts on the Association Between Thyroid Function and Metabolic Syndrome in Chinese. *Medicine*. 2015;94(50):e2193-e2193.
- <sup>22</sup>Morganti S, Ceda GP, Saccani M, et al. Thyroid disease in the elderly: sex-related differences in clinical expression. *J Endocrinol Invest*. 2005;28(11 Suppl Proceedings):101-104.
- <sup>23</sup>Samuels MH. Hyperthyroidism in aging. *Endotext* [Internet]. 2018.
- <sup>24</sup>Manji N, Carr-Smith JD, Boelaert K, et al. Influences of Age, Gender, Smoking, and Family History on Autoimmune Thyroid Disease Phenotype. *The Journal of Clinical Endocrinology & Metabolism*. 2006;91(12):4873-4880.