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Disease of the Thyroid Gland: A Histopathological Perspective

Innocent Emmanuel[1*], Mansur Ramalan Aliyu[2], Adam Ochigbo[1], Philip Akpa[1], Jagshak Barnabas Mandong[3] and Barnabas Mafala Mandong[1]

[1]Department of Histopathology, Jos University Teaching Hospital, Jos, Nigeria.
[2]Department of Internal Medicine, Aminu Kano Teaching Hospital, Kano, Nigeria.
[3]Federal Medical Center, Keffi, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author IE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AO, PA and JBM managed the analyses of the study. Authors MRA and BMM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The thyroid is affected primarily by disease conditions which are variously classified and are not uncommon worldwide. They could lead to enlargement of the thyroid gland thereby earning the designation "goiter". Globally, iodine deficiency has been identified as a major cause of goiter. This was a descriptive retrospective study of consecutive cases of thyroid specimen analyzed at the Histopathology Department of the Jos University Teaching Hospital, Jos, Nigeria, between January 2008 and December 2017. The aim of this work is to study thyroid disorders histologically, relating these findings to age and sex, and comparing same with previous reports.

The Hospital's Medical records and the Histopathology Departments served as sources for extraction of patient's data which included age, sex, and histological diagnosis. Archival slides were reviewed to confirm the diagnosis of the thyroid lesion.

Three hundred and eleven (311) cases of thyroid disease were diagnosed histologically at the Jos University Teaching Hospital during the study period. These lesions were broadly classified into developmental anomalies, hyperplasias, immune/inflammatory diseases, and neoplasm. They

**Corresponding author: Email: kinapele58@yahoo.com;*

accounted for 1.9% (6 cases), 81.3% (253 cases), 3.9% (12 cases), and 12.9% (40 cases) of all cases respectively. The age range of the study population was 1 year to 70 years, with a mean age of 41.2±12.0 SD, and peak incidence at 30 years to 39 years. There were 25 males and 286 females making a male female (M/F) ratio of 1:10.2.
Thyroid disorders are essentially a female disease in our environment occurring commonly in the third and fourth decade of life.

Keywords: Goiter; iodine; Jos.

1. INTRODUCTION

The thyroid is an important endocrine gland. It sits with its butterfly shape on the anterior neck region, lying on the larynx and trachea midway between the thyroid cartilage and the suprasternal notch, at the level of C5-T1 vertebrae [1,2].

It is affected primarily by disease conditions which are variously classified [1,3,4]. These pathologies can be resolved into four groups: developmental anomalies; inflammatory/immune disorders; hyperplasias; and neoplasias [5]. Thyroid disorders are not uncommon worldwide [6].They could lead to enlargement of the thyroid gland, thereby earning the designation “goiter” [7,8].

Globally, iodine deficiency has been identified as a major cause of goiter [9]. This has made the deficiency of this substance a major public health problem [9-11]. In 1998, it was reported that over 1/3rd of the world’s population are resident in iodine deficient areas [12]. In 2004, it was reported that at least 350million Africans are exposed to the risk of iodine deficiency [13].

Clinical manifestations of thyroid disorders are protean, but are similar in both benign and malignant cases [8]. Treatment could be medical, surgical, radioiodine, or combination therapy.

The aim of this work is to study thyroid disorders histologically, describing their spectrum, relating these findings to age and sex, and comparing same with previous reports.

2. METHODOLOGY

This was a descriptive retrospective study of consecutive cases of thyroid specimen analyzed at the Histopathology Department of the Jos University Teaching Hospital, Jos, Nigeria, between January 2008 and December 2017. The Hospital’s Medical records and the Histopathology Departments served as sources of patient’s data which included age, sex, and histological diagnosis. Archival slides were reviewed to confirm the diagnosis of the thyroid lesion. In cases of missing, broken or faded slides, archival tissue blocks were selected, sectioned into 5 µm slides, stained with haematoxylin and eosin, and reviewed microscopically to confirm the diagnosis of the disease. All histologically confirmed cases were included in the study, while those with inadequate records were excluded. We used SPSS statistical software to analyze the data and presented them in tables as simple frequencies and percentages.

3. RESULTS

Three hundred and eleven (311) cases of thyroid disease were diagnosed histologically at the Jos University Teaching Hospital during the study period. These lesions were broadly classified into developmental anomalies, hyperplasias, immune/inflammatory diseases, and neoplasms. They accounted for 1.9% (6 cases), 81.3% (253 cases), 3.9% (12 cases), and 12.9% (40 cases) of all cases respectively (Table 1 and 2).

The age range of the study population was 1 year to 70 years, with a mean age of 41.2$\pm$12.0 SD, and peak incidence at 30 years to 39 years. There were 25 males and 286 females making a male female (M/F) ratio of 1:10.2 (Table 1 and 2).

Thyroglossal cyst was the only developmental anomaly with an age range of 2 years to 45 years, mean age of 22.0±15.7 and peak incidence at 10 years to 19 years. There were 3 cases each of thyroglossal cyst in males and females (Table 1 and 2).

The commonest hyperplastic disease was simple multinodular goiter (SMG) amounting to 213 of cases, thereby accounting for 84.2% of hyperplasia, and 68.5% of all cases. It is therefore the commonest singular disease entity in this study. There were 12 males and 201 females with SMG with a M/F ratio of 1:16.8. Other hyperplastic diseases were Colloid goiter and Toxic goiter with 39 (12.5% of cases) and 1 (0.3% of all cases) case(s) respectively (Table 1 and 2).

Thyroiditis (Hashimoto) and Grave's disease accounted for 5(1.6%) and 6(1.9%) cases of all thyroid diseases. This translates to 41.7% and 50.05% of all immune/inflammatory diseases. The age range, peak incidence and mean of thyroiditis were 27-56 years, 50-59 years, and 40.6±12.5 SD respectively, while corresponding values for Grave's disease were 19-33 years, 30-39years, and 27.5±5.1 SD respectively. All 5 cases of thyroiditis were female, while 1 of the 6 cases of Grave's disease was male (M/F ratio 1:16.7). There was a case of Granulomatous thyroiditis (Table 1 and 2).

Follicular adenoma was the commonest neoplasm (18 cases) accounting for 45% of neoplasm, and 5.8% of all cases. It recorded an age range of 1-60 years, peak incidence at 30-39 years, and mean of 39.2±13.9 SD. There 5 males and 13 females (M/F ratio 1:2.4) with this neoplasm (Table 1 and 2).

Papillary carcinoma was slightly commoner than follicular carcinoma. They recorded 10 and 9 cases respectively accounting for 25.0% and 22.5% of neoplasms and 3.2% and 2.9% of cases respectively. They respectively had an age range of 32-65 years and 25-70 years; peak age of incidence of 30-39 years and 50-59 years; and mean age of 40.9±11.1SD, and 50.8±13.2. There were 2 male cases and 8 female cases of papillary carcinoma (M/F ratio 1:4). There was no male case of follicular carcinoma. There was 1 case each of medullary carcinoma, and poorly differentiated carcinoma (Table 1 and 2).

4. DISCUSSION

Hyperplastic lesions (goiter) are the commonest disorders of the thyroid gland in this study. This finding has been consistently reported by researchers [14-27]. We found simple multinodular goiter as the singular lesion with highest frequency of all hyperplastic lesions, and of the entire population, accounting for 68.5% of all thyroid lesions. Similar findings were recorded by Salami et al. (73.0%) [15], Chalya et al. (67.2%) [16], Der et al. (77.9%) [18], Solomon et al. (53.6%) [19], and Eke et al. (75.2%) [20].

Simple goiter results from an interplay of genetic susceptibility and environmental factors [28,29,30]. Iodine deficiency has been identified as the most important acquired trigger in this regard [9,28,31]. A study by Patel et al, demonstrated an increase in thyroid gland volume in Fischer rats fed low dose iodine diet [32]. Conversely, iodine supplementation has been shown to reduce thyroid/goiter volume [10,28,33]. One of the goals of the millennium development goals adopted by the United Nations was the elimination of iodine deficiency [34]. This led to the USI (Universal Salt Iodization) program, an intervention that gained the attribute of being an exceptional cost effective community health strategy [35]. This program was executed with reports of success across the globe in reducing goiter incidence [36,37,38]. Despite this, iodine deficiency still subsist [28,38].

Iodine deficiency is commonly associated with hilly or mountainous areas [39,40,41,42]. This is the attribute of the location of our center, as the designation "Plateau" was used to Christine this state that is located at the north-central part of Nigeria. Furthermore, some food substances (cabbage, broccoli, soya, and cauliflower) have been shown to interfere with uptake of iodine by neutralizing it [43]. These food substances are in abundance in our locality.

Goitrogenesis involves the hyperplasia and hypertrophy of thyroid parenchymal cells and connective tissue [32]. This is triggered by iodine deficiency. Other causative factors includes some drugs (e.g lithium and phenyl betazone), pituitary/thyroid hormone resistance, increased TSH receptor stimulation from pituitary tumors secretions, inborn errors of metabolism, exposure to radiations, smoking, increased BMI (body mass index), thyroid nodule, and female gender [43,44,45]. Ironically, iodine excess has also been reported to be goitrogenic [37,44,46,47,48,49,50,51,52].

Excess iodine intake has been associated with thyroid autoimmunity [53].This is an underlying pathologic mechanism of autoimmune thyroiditis (Hashimoto). Hashimoto thyroiditis has a low frequency of occurrencein this study accounting for 1.6% of all thyroid lesions. This low figure might not be unconnected with insufficiency of iodine in our locality (Plateau state, Nigeria) [30]. The rare occurrence of autoimmune thyroiditis was reported in most African studies [11,14,15,17,18,19,20,26,27,54,55]. Across Nigeria, Raheem et al. (Zaria), [14] Solomon et al. (Kano), [19] Salami et al. (Sagamu), [15] and Dodiyi-Manuel et al. (Port-Harcourt), [27] reported a frequency of 1.3%, 0.4%, 0.6%, and 1,3% respectively. Genetic factors have been suggested to be contributory to thyroid auto-antibodies in Africa [56]. Lower levels of these auto-antibodies were established in black Africans than Africans of European and Asian descent [57].

Table 1. Age distribution of thyroid lesions

Diagnosis/Disease	Age (Years)								Total (%)
	<10	**10-19**	**20-29**	**30-39**	**40-49**	**50-59**	**60-69**	**70 -79**	
Developmental anormalies									
Thyroglossal cyst	1	2	1	1	1	-	-	-	6(1.9)
Hyperplasia									
Simple multinodular goiter	-	2	20	66	68	38	14	5	213(68.5)
Colloid goiter	0	1	8	11	11	6	1	1	39(12.5)
Toxic Goiter	-	-	1	-	-	-	-	-	1(0.3)
Inflammatory/Immune									
Thyroiditis (Hashimoto)	-	-	1	1	1	2	-	-	5(1.6)
Grave's disease	-	1	2	3	-	-	-	-	6(1.9)
Granulomatous thyroiditis		-	-	-	-	-	1	-	1(0.3)
Neoplasia									
Benign Neoplasm									
Follicular adenoma	1	-	1	6	5	4	1	-	18(5.8)
Hurtle cell adenoma	-	-	-	-	-	1	-	-	1(0.3)
Malignant Neoplasm									
Papillary carcinoma	-	-	1	6	1	1	1	-	10(3.2)
Follicular carcinoma	-	-	1	-	-	7	-	1	9(2.9)
Medullary carcinoma	-	-	1	-	-	-	-	-	1(0.3)
Poorly differentiated carcinoma	-	-	-	1	-	-	-	-	1(0.3)
Total	2	6	37	95	87	59	18	7	311(100.0)

Table 2. Gender and age distribution of thyroid disease

Diagnosis/disease	Number of case (%)	Gender		Age (Years)		
		M	F	Age range	Peak age	Mean
Developmental anormalies						
Thyroglossal cyst	6(1.9)	3	3	2-45	10-19	22.0±15.7
Hyperplasia						
Simple multinodular goiter	213(68.5)	12	201	13-70	40-49	42.5±11.3
Colloid goiter	39(12.5)	2	37	18-49	30-39/40-49	40.8±8.3
Toxic Goiter	1(0.3)	-	1	-	-	24.0
Inflammatory/immune						
Thyroiditis (Hashimoto)	5(1.6)	-	5	27-56	50-59	40.6±12.5
Grave's disease	6(1.9)	1	5	19-33	30-39	27.5±5.1
Granulomatous thyroiditis	1(0.3)	-	1	-	-	61
Neoplasia						
Benign Neoplasm						
Follicular adenoma	18(5.8)	5	13	1-60	30-39	39.2±13.9
Hurtle cell adenoma	1(0.3)	-	1	-	-	50.0
Malignant Neoplasm						
Papillary carcinoma	10(3.2)	2	8	32-65	30-39	40.9±11.1
Follicular carcinoma	9(2.9)	-	9	25-70	50-59	50.8±13.2
Medullary carcinoma	1(0.3)	-	1	-	-	22.0
Poorly differentiated carcinoma	1(0.3)	-	1	-	-	37.0
Total	311(100.0)	25	286	1-70	30-39	41.2±12.0

Thyroglossal cyst is a developmental anomaly occurring in the thyroid gland. It is the only developmental anomaly seen in this study. It is also the lone congenital anomaly of the gland reported by other researchers [14,19,20,25,26]. Although thyroglossal duct cyst is reported as having a low frequency, our study recorded a figure as lower as 1.9% of all thyroid pathologies. Raheem et al. (Kano), Salami et al. (Sagamu), Solomon et al. (Kano), Eke et al. (Abuja), Ijomone et al. (Port Harcourt) reported a frequency of 5.7%, 2.2%, 6.9%, 9.2%, and 5.3% respectively for thyroglossal cyst in this regard [14,15,19,20,25].

Malignant thyroid neoplasms (21.0%) were commoner than benign (19.0%) neoplastic proliferations. This finding was corroborated byChalya et al, and Bhaita et al. [16,17]. However many other researchers reported a preponderance of benign neoplasm [14,15,18,19,20,25,26]. Dodiyi-Manuel et al reported an equal frequency of occurrence ofthese two broad classesof neoplasia [27].

Malignant neoplasms are by far the most important histopathologic diagnostic entity, and the commonest reported in the thyroid are carcinomas. Thyroid cancer is the commonest endocrine malignancy [58,59]. Worldwide, it's incidence has been increasing [44,60]. Papillary carcinoma and follicular carcinoma are the commonest cancers in this study accounting for 3.2% and 2.9% of all thyroid lesions. The predominance of these cancers over other subtypes was corroborated by many researchers across Africa [11,14,15,18,26,27,54,55,61-67]. The frequent occurrence of papillary thyroid cancer in our study over follicular carcinoma was similar to reports by some researchers [14,18, 26,27,11,63,67]. Other researchers reported the reverse [16,54,55,61,64,65,66]. The reason for this discrepancy within the same continent has not yet been fully elucidated. However, iodine deficiency has been associated with follicular carcinoma [61], while iodine supplementation (sufficiency) has been linked to papillary thyroid carcinoma [68]. The rising incidence of thyroid carcinoma has been attributed to increase in papillary thyroid carcinoma [69]. This might not be unconnected with the drive towards iodine sufficiency through the USI program lunched across the globe. More studies are needed to trail a possible change in pattern of thyroid carcinoma from follicular to papillary subtype in our environment.

To the best of our knowledge, reported studies across the globe showed a preponderance of female over males in the incidence of thyroid diseases. Our study is no exceptions as there were 25 males and 286 females making a male female ratio of 1:10.2. A similar wide gap has been reported by researchers [14-21,25-27, 63,69,70]. Future prospects of studying the possible stimulatory effects of estrogen or estrogen like hormone, or the inhibitory influence of male sex hormones on the thyroid towards the development of disease in the gland is worthwhile.

We found 58.5% (182) cases of thyroid lesions occurring within the third and fourth decade (30 to 49 years). Salami et al (Sagamu), Solomon et al (Kano), and Eke et al. (Abuja), documented similar findings for this age range, as it accounted for 57.2%, 54.8%, and 54.0% respectively for all thyroid lesions [15,19,20]. Raheem et al. (Zaria) and Dodiyi-Manuel et al. (Port Harcourt), similarly found the age group 30-50 years accounting for 56.2% and 52.5% respectively [14,27]. Ijeomone et al (Port Harcourt), however differ from these, reporting the class 21-40 years as the age group with the highest frequency (63.9%) [25].

5. CONCLUSION

Thyroid disorders are essentially a female disease in our environment occurring commonly in the third and fourth decade of life. It is linked to iodine deficiency which is associated with some factors like high altitude and goitrogenic diets, which are attributes of our environment. Multinodular goiter is by far the commonest pathology of the gland in our locality and papillary carcinoma is the most frequent malignancy.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Standring S, Ellis H, Healy JC, Johnson D, Williams A, Eds. Gray's anatomy. 39th Ed. Philadelphia: Saunders and Elsevier. 2005;462-4.
2. Bychkov Andrey. The thyroid gland. Pathology outlines.com. Available:http://www.pathologyoutlines.com/topic/thyroidanatomy.html (Retrieved on 01/05/2018)
3. Maitra M. The endocrine system. In, Kumar V, Abbas AK, Fausto N, Editors. Pathologic Basis of Disease. 8th Ed. Philadelphia: Saunders and Elsevier. 2010;1082‑1105.
4. Walsh PJ. Managing thyroid disease in general. MJA. 2016;205(4):179-184.
5. Der EM, Quayson SE, Clegg-Lamptey JN, Wiredu EK, Ephraim RKD, Gyasi RK. Thyroid disorders in Accra Ghana: A retrospective histopathological study at the Korle-Bu Teaching Hospital. J Med Biomed Sc. 2013;2(1):1-7.
6. Vanderpump MPJ, Tumbridge WMG. The epidemiology of thyroid doseases. In: Braverman LE, Utiger RD, Eds. The Thyroid. 7th Ed. Philadelphia: Lippincott Raven. 1996;476-82.
7. Huang MJ, Liaw YF. Clinical association between thyroid and liver disease. J Gastroenterol Hepatol. 1995;10:344-50. Available:http://dx.doi.org/10.111/j.1440-1746.1995.tb01106.x PMID: 754881
8. Constantinidis V, Palazzo F. Goitre and thyroid cancer. Med J. 2013;4(9):546-50.
9. Triggiani V, Tafaro E, Giagulli VA, Sabba C, Resta F, Licchelli B, Guastamacchia E. Role of iodine, selenium and other micronutrients in thyroid function and disorders. Endocr Metab Immune Disord Drug Target. 2009;9(3):277-94.
10. Wijeyarante CN, Jayasinghe A, de Silva DGH, Parkes AB, Lazarus JH, Premawardhana LD. Iodine prophylaxis, goiter and thyroid autoimmunity in Sri Lanka. Ceylon Med J. 2005;50(1):20-3.
11. Tsengaye B, Egrete W. Histopathological pattern of thyroid diseases. East Afr Med J. 2003;80-525-8.
12. WHO, UNICEF and ICCIDD. Progress towards elimination of iodine deficiency disorders (IDD). WHO, Geneva; 1999.
13. World Health Organization. Iodine status worldwide: WHO Global database on Iodine deficiency. Geneva: WHO. 2004;1-58. Available:www.whqlibdoc.who.int/publications/2004/9241592001.pdf (Retrieved on 10/01/2016)

14. Raheen N, Ahmed SA, Samaila MOA. Histopathological pattern of thyroid diseases in Zaria: A 10 year review. Niger Post Med J. 2018;25:37-42.
15. Salami BA, Odusan O, Ebili HO, Akintola PA. Spectrum and prevalence of thyroid diseases seen at a tertiary health facility in Sagamu, South-West Nigeria. Niger Postgrad Med J. 2016;23:137-40.
16. Chalya PL, Rambau P, Mabula JB, Kanumba ES, Giiti G, Chaadika AB, et al. Tanzania J Health Res. 2011;11(3):1-9.
17. Bhaita S, Mahajan S, Kaur M, Kansal P. Thyroid swellings-A common problem in hilly areas. JDMS. 2014;13(5):88-90.
18. Der EM, Quayson SE, Clegg-Lamptey JN, Wiredu EK, Ephraim RKD, Gyasi RK. Thyroid disorders in Accra, Ghana: A retrospective histopathological study at the Korle-Bu Teaching Hospital. J Med Biomed Sc. 2013;2(1):1-7.
19. Solomon R, Illiyasu Y, Mohammed AZ. Histopathological pattern of thyroid lesions in Kano, Nigeria: A 10 year retrospective review (2002-2011). Niger Med Basic Clin Sci. 2015;12:55-60.
20. Eke B, Ojo BA, Duduyemi BM, Ugwu IV, Omobong EO, Shorun G, Okolie I. Histopathological pattern of thyroid disease in Abuja, Nigeria capital city. A review of one hundred one consecutive cases. IJTDH. 2017;21(3):1-5.
21. Modi M, Daveshwar M. Study of histopathological pattern of thyroid lesions. Int J Biomed Advance Res. 2018;9(1):27-36.
22. Darwish HA, Al Sindi HA, Kafsi JE, Acantab B. Pattern of thyroid diseases- A histopathological study. Bahrain Med Bulltin. 2006;28(4):1-6.
23. Salama SI, Abdullah LS, Al-Qahtani MH, Al-Maghrabi JA. Histopathological pattern of thyroid lesions in western regions of Saudi Arabia. New Egypt J Med. 2009;40(6):580-5.
24. Nazul HSM, Idrish AM, Mahmudul HM, Fatah RSN, Addus SM, Mohiuddin KA. Histopathological pattern of malignancy in solitary thyroid nodule. Bangladesh J Otorhinolaryngol. 2012;18(1):5-10.
25. Ijomone EA, Duduyemi BM, Udoye E, Nwosu SO. Histopathological review of thyroid diseases in Southern Nigeria- a ten year retrospective study. J Med Sci. 2014;5(6):127-32.
26. Rahman MA, Biswas MA, Siddika ST, Sikder AM, Talukder SI, Almagir MH. Histomorphological pattern of thyroid lesions. Dinajpur Med J Col J. 2012;6(2): 134-40.
27. Dodiyi-Manuel A, Dodiyi-Manuel ST. Spectrum of thyroid diseases in the surgical department of a tertiary center in South-South, Nigeria. Niger Health J. 2016;16(2):19-27.
28. Fast S, Nielsen VE, Bonnema SJ, Hegedus S. Time to reconsider non-surgical therapy of benign non-toxic multinodular goiter: Focus on recombinant human TSH augmented radioiodine thewrapy. Eur J Endocrinol. 2009;160:517-528.
29. Koutras DA. Variation in incidence of goiter within iodine-deficient populations. In, Endemic goiter and cretinism continuing threats to world health. EdsDunn JT, Meindeiros-Neto G. Washington DC: PAHO Science Publishers. 1974;95-101.
30. Isichei UP, Morimoto I, Das SC, Egbuta O, Banwo AI, Nagataki S. Endemic goiter in the Jos Plateau region of Norther Nigeria. Endocr J. 1995;42(1):23-9.
31. Hetzel BS. Iodine deficiency disorder (IDD) and their eradication. Lancet. 1983;2:1126-9.
32. Patel VA, Hill DJ, Sheppard MC, Wang JF, Logam A, Eggo MC. Apoptosis during goiter involution- the role of BCL2. J Endocrinol. 2000;164:323-30.
33. Hintze G, Kobberling J. Treatment of iodine deficiency goiter with iodine, levothyroxine or a combination of both. Thyrodology. 1992;4:37-40.
34. Sustainable elimination of iodine deficiency: Progress since the 1990 world summit for children. New York: United Nations Children's Fund.
Available:http:childreninfo.org/files/idd-sustainable-elimination.pdf
(Accessed 10/01/2016)
35. Pearce EN, Anderson M, Zimmerson MD. Global iodine nutrition: Where do we stand in 2013? Thyroid. 2013;23:523-8.
36. Grimaldi A, Kakande B, Narayana K, Sebalta E, Trucco G, Mirabel M, et al. Neck mass in Rural Africa. Clinical communication to the editor. Am J Med. 2015;128(2).
37. Zhao W, Hanc C, Shi X, Xiong C, Sun J, Shan Z, et al. Prevalence of goiter and thyroid nodules before and after implementation of the universal iodization program in mainland China from 1985 to 2014: A systematic review and meta-

analysis. PLOS ONE. 2014;9(10): e109549.
DOI: 10.1371/journal.pone.0109549

38. Yadau S, Gupta SK, Godbole MM, Jain M, Singh U, Pavithran VP, et al. Persistence of severe iodine-deficiency disorders despite universal salt iodization in an iodine deficient area in Northern India. Public Health Nutr. 2010;13:424-9.
39. Delange F. Disorders induced by iodine deficiency. Thyroid. 1994;4(1):107-28. Available:https://doi.org/10.1089/thy.1994.107
40. Abuye C, Berhane Y, Ersumo T. The role of changing diet and altitude on goiter prevalence in five regional states in Ethiopia. East Afr J Public Health. 2008;5: 163-8.
41. Abu-Eshy SA, Abolfolouh MA, Al-Naggar YM. Endemic goiter in school children in high and low altitude areas of Asir region, Saudi Arabia. Saudi Med J. 2001;22:146-9.
42. Harris NS, Crawford PB, Yangzom Y, Pizino L, Gyaltsen P, Hudes M. Nutritional and health status of Tiebetan children living at high altitudes. N Eng J Med. 2001;344:341-7.
43. Nnodim J, Emejulu A, Elendu HN. Evaluation of serum hepatocellular enzymes in Nigerian with goiter. AJMS. 2011;2:79-81.
44. Gherbon A. Epidemiological aspects of euthyroid diffuse goiter in a group of adults with thyroid diseases and diabetes mellitus and other changes in glycerine balance. Eur Sc J. 2015;11(3):29-39.
45. Dauksiene D, Petkeviciene J, Klumbiene J, Verkauskiene R, Vainikonyle K, Seibokaite A, et al. Factors associated with the prevalence of thyroid nodules and goiter in middle aged euthyroid subjects. Int J Endocrinol. 2017;8401518.
DOI: 10.1155/2017/8401518
46. Pearce EN, Gerber AR, Gootnick DB, Khan LK, Li R, Pino S, et al. Effects of chronic iodine excess in a cohort of long-term American workers in West Africa. J Clin Endocrinol Metab. 2002;87:5499-502.
47. Yu JS, Shan ZY, Chong W, Mao JY, Geng YX, Zhang C, et al. Vitamin E ameliorates iodine-induced cytotoxicity in thyroid. J Endocrinol. 2011;209:299-306.
48. Zhao J, Wang P, Shang L, Sullivan KM, van der Haar F, Maberly G. Endemic goiter associated with high iodine intake. Am J Public Health. 2000;90(10):1633-5.
49. Liu P, Liu L, Shen H, Jia Q, Wan J, Zheng H. The standard intervention measures and health risk for high water iodine areas. PLoS ONE. 2014;9(2):e89608.
50. Namba H, Yamashita S, Kimura H, Yokoyama N, Usa T, Otsuru A. Evidence of thyroid volume increase in normal subjects receiving excess iodine. J Clin Endocrinol Metab. 2014;76:605-8.
51. Lemar HJ, Georgitis WJ, McDermott MJ. Thyroid adaptation to chronic triglyceride hydroperiodide water purification tablet use. J Clin Endocrinol Metab. 1995;80: 220-3.
52. World Health Organization, United Nation Children's Fund. International council for the control of iodine deficiency disorders and monitoring their elimination: A guide for program managers. Geneva, Switzerland: World Health Organization; 2007.
53. Doufas AG, Mastorakos G, Chatziioannou S, Tseleni-Balafouta S, Piperingos G, Boukis MA, et al. Eur J Endocrinol. 1999;140:505-11.
54. Olurin, Itayemi SO, Oluwasanmi JO, Ajayi OO. The pattern of thyroid gland disease in Ibadan. Niger Med J. 1973;3:58-65.
55. Gitau W. An analysis of thyroid diseases seen at Kenyatta National Hospital. East Afr Med J. 1975;52:564-70.
56. Okosieme OE. Impact of iodination on thyroid pathology in Africa. J R Soc Med. 2006;99:396-401.
57. Kalk WJ, Kalk J. Incidence and causes of hypothyroidism in blacks. S Afr Med J. 2011;75:114-17.
58. Frelay J, Soerjomataram I, Ervick M, Dikshit R, Eser S, Mathers C, et al. GLOBOCOM 2012 v 1.0, cancer incidence and mortality worldwide: IARC cancer base. NO 11 (internet). Lyon France: International Agency for Research on Cancer; 2013.
Available:http://globocan.iarc.fr
(Accessed on 10/01/2016)
59. Siegel R, Naishadham D, Jamal A. Cancer statistics, 2012. CA Cancer J Clin. 2012;62(1):10-29.
60. Sharma R, Bharti S, Kumar KH. Diets and thyroid-myths and facts. J Med Nutr Nutriceut. 2014;3(2):60-5.
61. Lawal O, Agbakwuru A, Olayinka OS, Adelusola K. Thyroid malignancy in endemic nodular goiters. Prevalence, pattern, and treatment. J Cancer Surg Oncol. 2001;27(2):157-161.

62. Thomas JO, Ogunbiyi JO. Thyroid cancers in Ibadan, Nigeria. East Afr Med J. 1995;72:231-3.
63. Ukekwe F, Olusina DB, Okere PCN. Pattern of thyroid cancers in South Eastern Nigeria: A 15 year histopathological review (2000-2014). J Clin Diagnostic Res. 2017;11(8):16-19.
64. Mulaudzi TV, Ramdial PK, Madiba TE, Callaghan RA. Thyroid carcinoma at King Edward VIII Hospital, Durban, South Africa. Eat Afr Med J. 2001;78(5):242-5.
65. Selzer G, Khan LB, Albertyn L. Primaty malignant lesions of the thyroid gland: A clinicopathologic study 254 cases. Cancer. 1977;40:1501-10.
66. Omran M, Ahmed ME. Carcinoma of the thyroid in Kartoum. East Afr Med J. 1993;70:159-62.
67. Bakiri F, Djemli FK, Mokrane LA, Djidel FK. The relative roles of endemic goiter and socioeconomic development status in the prognosis of thyroid carcinoma. Cancer. 1998;82:1146-53.
68. Harach HR, Williams ED. Thyroid cancer and thyroiditis in the goitrous region of Salta, Argentina, before and after iodine prophylaxis. Clin Endocrinol. 1993;43:701-6.
69. American Cancer Society. Cancer facts and figures; 2016.
Available:https://www.cancer.org/research/cancer-fcts-statistics/all-cancer-facts-figures/cancer-facts-figures-2016.html
(Accessed 10/01/2016)
70. Meredith I, Sarfati D, Atkinson J, Blakely T. Thyroid cancer in pacific women in New-Zealand. NZMJ. 2014;127(1395):52-62.

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