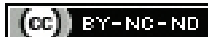


Contributing Factors of Hypothyroidism- A Systematic Review

SALINA SUNIL¹, KC LEENA²

ABSTRACT

Introduction: Hypothyroidism is an emerging public health concern, which need to be of due significance. In spite of iodine supplementation started three decades ago, hypothyroidism is still a problem to be tackled. Apart from iodine deficiency, the contributing factors of hypothyroidism have to be explored.

Aim: To identify the contributing factors of hypothyroidism in adults.

Materials and Methods: A systematic literature search was done using PubMed, MEDLINE, Embase, Google Scholar and the internet search from 2000 to 2018. The key words used were hypothyroidism, thyroid disorders, underactive thyroid, contributing factors, causes and associative factors. All the articles were analysed and the data were extracted using eligibility (inclusion and exclusion criteria) criteria. A total of 14 articles, which are either review articles or systematic reviews, in English language, and are fully retrievable were analysed and a systematic review was performed. Among the reviews, nine were review analysis and five were systematic reviews. The risk of bias

assessment was done at the study level and data synthesis was done based on the criteria satisfied by the checklist.

Results: The present analysis has included studies related to contributing factors of hypothyroidism. The analysis revealed the following contributing factors of hypothyroidism. Too little or too much iodine (43%), excess fluoride (7%), female gender (14%), presence Thyroid Peroxidase (TPO) antibodies (36%), smoking status (14%), age above 70 years (21%), unregulated use of pesticides (14%), contaminated drinking water (14%), certain medicines (29%), use of plastic bottles contain Bisphenol A (BPA) and paper cups insulated with plastics (7%) and exposure to goitrogens (7%).

Conclusion: Hypothyroidism is a leading emerging health problem in India. The prevalence is 11-15%. Despite the fact iodine fortification since 1983, hypothyroidism is a major public health to be tackled. In the current review five studies from India were included. Most of the studies showed the iodine as the contributing factor either in too much level or too little level.

Keywords: Autoimmune disorders, Iodine deficiency, Iodisation, Thyroid problems

INTRODUCTION

Thyroid gland is situated in front of the neck, anterior to the trachea. Embryologically, it arises from a midline invagination at the root of the tongue and grows downwards in front of trachea, and thyroid cartilage to reach its normal position. It is a bilobed structure. Thyroid is made up of follicles containing colloid. Thyroid gland produces two hormones tri-iodothyronine (T3) and Thyroxine (T4). These hormones are formed through series of enzymatic processes starting with trapping of iodine from blood. Thyroid hormones are responsible for the control of most labile organs in the body and responds to numerous stimuli such as puberty, pregnancy, physiologic stress and various pathologic states [1,2]. Hypothyroidism is a hypo metabolic clinical state resulting from inadequate production of thyroid hormones for prolonged periods or rarely from resistance of the peripheral tissues to the effects of thyroid hormones. The clinical manifestations can be cretinism or congenital hypothyroidism and myxoedema [1,2].

Causes of hypothyroidism are numerous. Developmental anomalies, genetic defect, foetal exposure to iodine and antithyroid hormones, endemic cretinism lead to congenital hypothyroidism. Ablation of thyroid by surgery or radiation, autoimmune thyroiditis, endemic goitre, hypothalamic pituitary lesions, thyroid cancers, prolonged administration of antithyroid drugs lead to myxedema or adult hypothyroidism [1,2].

Prevalence of hypothyroidism is increasing worldwide. Hypothyroidism is the most common thyroid disorders in India, affecting one in ten adults. The prevalence is 11%, compared with 2% in UK and 4.6% in USA [3].

Iodised salt is strongly recommended in India since 1983. According to recent statistics (2014), there is high prevalence of hypothyroidism in India. The prevalence was around 11%. In India, patients with hypothyroidism are undetected and most of the time untreated also.

Hypothyroidism is easy to detect and treatment is inexpensive. Most of the time hypothyroidism affects the overall quality of life and it in turn affect the work performance and productivity of the individuals affected. In the past, iodine deficiency was blamed for the occurrence of hypothyroidism in India, but the disease is still prevalent in this country, despite the promotion of iodised salt since 1983 [4].

The present systematic review attempts to find the contributing factors for the increasing incidence of hypothyroidism. Iodine deficiency was blamed for the occurrence of hypothyroidism. Universal Salt Iodisation (USI) was adopted by the World Health Assembly in 1994. However, the incidence of hypothyroidism is growing year by year [5].

There can be other factors which contribute to the development of hypothyroidism. The present systematic review searched for major contributing factors of the hypothyroidism.

MATERIALS AND METHODS

The systematic review was carried out from February 2019 to July 2019 according to the guidelines of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement.

Search strategy: A systematic literature search was done using PubMed, MEDLINE, Embase, Google Scholar and the internet search. Only articles in English language were searched. The search was done which included published studies, which dealt with causes, contributing factors, associative factors of hypothyroidism from 2000-2018. The key words were hypothyroidism, thyroid disorders, underactive thyroid, contributing factors, causes and associative factors. Out of total search of articles related to hypothyroidism, there was a mixture of studies like case controls, systematic reviews, cross-sectional studies and review articles. For these categories of studies, studies in general population were included.

Inclusion criteria:

1. Only in English language
2. Articles which are fully available/retrievable
3. Related to review of hypothyroidism and systematic review

Exclusion criteria:

1. Articles with only abstracts
2. Web news congenital studies

For these categories of studies, studies in the general adult population, demographic segment of adult population or among patients in general clinic setting were included. Two principal investigators were involved in retrieving, analysing and evaluation of articles and it was sorted out.

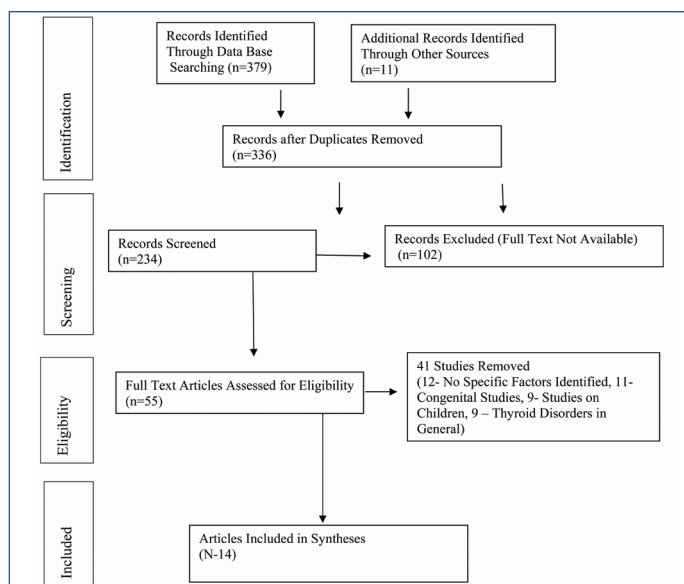
Initially, 379 abstracts from different data base and 11 text book contents were identified. Total 54 duplicates abstracts were removed with further screening. Subsequent screening identified 102 abstracts in which full text were not available and those were removed. Further 55 full text articles were reviewed. Out of these articles, 11 were congenital studies, nine studies were done on children, nine studies were concerned with thyroid disorders in general and 12 studies have not identified specific factors contributing to hypothyroidism. So, 41 full text articles were removed and for final screening 14 articles were included; out of these five were systematic reviews, six were review articles and three editorials which are of significant in identifying contributing factors were included [Table/Fig-1].

The identification, screening and checking for eligibility criteria were done separately by two investigators and final review, synthesis and analysis was done together by both investigators.

Data Extraction

Data extraction was done by the two investigators separately. The identification, screening and checking for eligibility criteria were done separately by two investigators. All the articles were analysed and the data were extracted using eligibility (Inclusion and exclusion criteria) criteria. Data from three editorials were considered. They are from American Thyroid Association, National Health System (UK) and Down to earth. These were included owing to the significance of the content which contributes to the overall quality of the systematic review.

A total of 14 articles that met the eligibility criteria were analysed and a systematic review was performed. The risk of bias assessment was done with Joanna Brigs Institute (JBI) critical appraisal checklist



[Table/Fig-1]: Flow chart of the study characteristics identified in the study.

for systematic review [6] and for review article the methodology and the number of articles included were taken care of. The JBI critical appraisal checklist is included in [Table/Fig-2] [7-11].

STATISTICAL ANALYSIS

The risk of bias assessment was done at the study level and data synthesis was done based on the criteria satisfied by the checklist.

RESULTS

The results of search strategies are presented in [Table/Fig-3] [3,4,7-18] stating the characteristics identified in the study and analysis of various studies employed in the systematic review. The present analysis has included studies related to contributing factors of hypothyroidism. It tried to associate hypothyroidism with various factors. A total of 14 studies fulfilled inclusion criteria. Among them 9 were review analysis and 5 were systematic review. The analysis revealed the following factors: too little or too much iodine, excess fluoride, female gender, presence TPO antibodies, smoking status, age above 70 years, unregulated use of pesticides, contaminated drinking water, certain medicines, use of plastic bottles containing BisPhenol A (BPA) and paper cups insulated with plastics and exposure to goitrogens. It is presented in [Table/Fig-4,5].

S. No.	Criteria	Chaitanya NCSK [7]				Ankim Y and Park YJ [8]				Vestergarrel P [9]				Yuan J et al., [10]				Ning Y et al., [11]			
		Y	N	U	NA	Y	N	U	NA	Y	N	U	NA	Y	N	U	NA	Y	N	U	NA
1	Is the review question clearly and explicitly stated?	x				x				x				x				x			
2	Were the inclusion criteria appropriate for the review question?	x				x				x				x				x			
3	Was the search strategy appropriate?	x				x				x				x				x			
4	Were the sources and resources used to search for studies adequate?	x				x				x				x				x			
5	Were the criteria for appraising studies appropriate?	x				x				x				x				x			
6	Was critical appraisal conducted by two or more reviewers independently?	x							x				x					x			
7	Were there methods to minimise errors in data extraction?	x				x				x				x							x
8	Were the methods used to combine studies appropriate?			x				x		x				x				x			
9	Was the likelihood of publication bias assessed?	x				x				x				x							x
10	Were recommendations for policy and/or practice supported by the reported data?		x			x					x				x			x			
11	Were the specific directives for new research appropriate?		x				x				x				x			x			

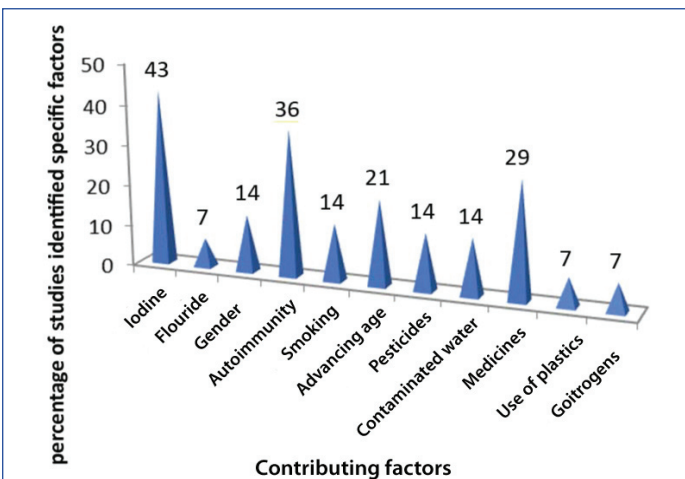
[Table/Fig-2]: Joanna Brigs Institute (JBI) critical appraisal checklist for systematic reviews [7-11]. Y: Yes; N: No; U: Unclear; NA: Not clear

3.a Description and results of systematic reviews.				
Author reviewed	Year	No. of articles	Rationale for review	Results obtained
Chaithanya NCSK et al., [7]	2018	10	Compilation of evidences for providing relation with fluoride and thyroid disorders.	Positive correlation is found between fluoride and thyroid disorders.
Ankim Y and Park YJ [8]	2014	14	To collect evidences for relation between iodine rich geographical area and incidence of Hypothyroidism.	High iodine intake, age, women Presence of TPO Ab and smoking status contribute to Hypothyroidism.
Vestergarrel P [9]	2002	25	Review had done to know the possible relation of smoking to autoimmunity.	Stastical significance of smoking is identified. Hashimoto thyroiditis, radioactive iodine is related to Hypothyroidism.
Yuan J et al., [10]	2018	54	Review had been done to assess the association between thyroid disorders and vitiligo.	Hypothyroidism is prevalent in vitiligo patients.
Ning Y et al., [11]	2017	55	Review the evidences to find out relation between Cardiovascular risk and Hypothyroidism.	Cardiac diseases are risk factor to Hypothyroidism.

3.b Description and results of reviews (including editorials).				
Name of reviewer	Year	Site of publication	Rationale for review	Results
Editorial* [3]	2018	Down-to-earth	To explain the additional factors leading Hypothyroidism apart from iodine deficiency	Age over 60 years, unregulated use of pesticides, exposure to endocrine disruptors, contaminated water, industrial pollutants and iodine deficiency was identified as factors autoimmunity, unregulated use of pesticides, goitrogens, exposure to Endocrine disruptors, unclean drinking leading to Hypothyroidism Autoimmunity, thyroid removal iodine deficiency, radioactive iodine and surgery are identified as factors leading to hypothyroidism hashimoto thyroiditis, radiation treatment, certain drugs (lithium, interleukins, interfeons, amiodarone) Autoimmunity, surgical removal of thyroid gland, radiation treatment, drugs, too much or too little iodine, damage to pituitary gland
Bagochi S [4]	2014	The Lancet	To explore the various factors that may contribute to the incidence of Hypothyroidism	
Mathur R [12]	2018	Medicine Net	Review various factors leading to Hypothyroidism	
Wartofsky L [13]	2016	NIDDK	Explore the various factors leading to Hypothyroidism	
Editorial* [14]	2018	American thyroid association	Review common causes of Hypothyroidism apart from Hashimoto disease	
McIntosh J [15]	2018	MNT	To give a comprehensive information about Hypothyroidism	
American Thyroid Association [16]	2013	American thyroid association	To highlight the factors leading to Hypothyroidism to patients and their family	
Kharrazian D [17]	2014	Dr K News	To explore role of environmental triggers and plastics in the incidence of Hypothyroidism	
Editorial* [18]	2018	NHS (UK)	To explore and identify various factors that may contribute to Hypothyroidism	
				Use of plastic containing BPA, plastic coffee lids, drinking bottles, paper cups might contribute to Hypothyroidism
				Immune system, previous thyroid treatment, diet low in iodine, medicines like lithium, amiodarone, interferons

[Table/Fig-3]: Analysis of various studies employed in the systematic review [3,4,7-18].

*editorial has been added since the data contribute significantly to the purpose of current review



[Table/Fig-4]: Cone diagram showing contributing factors by percentage.

Smoking status	Ankim Y and Park YJ [8], Vestergarrel P et al., [9]	Tobacco smoking causes variation in thyroid immunity.
Advancing Age	Ankim Y and Park YJ [8], Down-to-earth [3], American Thyroid association [16]	Hypothyroidism is more common among people over 60 years when compared to younger age
Unregulated use of pesticides	Down-to-earth [3], Kharrazian D [17],	Pesticides are endocrine disruptors. They interfere in the thyroid pathways and effects Hypothalamic-Pituitary-Thyroid axis at various levels
Contaminated drinking water	Down-to-earth [3], Bagochi S [4]	Contaminated water loosely affects thyroid health
Certain medicines (Interleukin 2, lithium, Inerferon α, amiodarone)	Wartofsky L [13], American Thyroid association [14], NHS (UK) [18]	Amiodarone cause inhibition of secretion of T3 and T4. Interleukin 2 causes thyroiditis. Lithium causes autoimmunity and hypothyroidism
Use of Plastics	Bagochi S [4]	BisPhenol A has got endocrine disruptive effects and affects thyroid health.
Goitrogens	Bagochi S [4]	Cruciferous vegetables act as goitrogens and affects thyroid health. Consumption of these vegetables on long term affects thyroid gland.

[Table/Fig-5]: Contributing factors of hypothyroidism [3,4,7-18].

Contributing factors	Evidence/Literature sources	Conclusion
Iodine	Ankim Y and Park YJ [8], Down-to-earth [3], Mathur R [12], American Thyroid association [14], American Thyroid association [16], NHS (UK) [18]	Too much iodine causes thyroid autoimmunity and too little iodine cause under activity of thyroid gland
Excess fluoride	Chaithanya NCSK [7]	Flouride has an anti-inhibitory effect upon thyroid gland
Female gender	Ankim Y and Park YJ [8], American Thyroid association [16]	Menopause cause females more prone to get hypothyroidism
Presence of TPO antibodies	Ankim Y and Park YJ [8], NHS (UK) [18], Mathur R [12], American Thyroid association [14], Bagochi S [4], American Thyroid association [16], NHS (UK) [18],	TPO antibodies act against self-structures and there is aggravated cytotoxic action of T cells

DISCUSSION

Factors leading to hypothyroidism are hashimoto thyroiditis, problems with thyroid itself (surgical removal, congenital thyroid agenesis or the destruction of thyroid by radioactive iodine as in case of thyroid cancer), medications (amiodarone prescribed for arrhythmias, antithyroid medications, interferon alpha prescribed

for certain malignancies or those with hepatitis B or hepatitis C, interleukin-2 prescribed for metastatic cancers and leukaemia, lithium for depression or bipolar disorders), abnormal growth in the Thyroid gland, problems in the pituitary like tumour, and genetic defects. Increased iodine intake, selenium, Vitamin D deficiency, exposure to radiation are some of the environmental factors increases autoimmunity [19].

A prospective population study done in Denmark explored the incidence of overt hypothyroidism after iodine fortification. Study states that one of the main complications observed after initiation of iodine prophylaxis is iodine induced hyperthyroidism which has been reported in many iodine supplementation programme [20]. Worldwide there are many such programmes like Universal Salt Iodisation (USI) which was adopted by Joint United Nations Children's Fund/World Health Organisation (UNICEF/WHO) committee on Healthy Policy [21], National Iodine deficiency programme by Government of India in 1962 [22]. In this prospective epidemiological study of a cohort representative of the Danish population performed before and during the first 7 year of iodine fortification of salt in Denmark, it was found that the overall incidence rate of hypothyroidism increased significantly during the period of mandatory iodine fortification. It was a prospective study, and there were no control groups who have a stable iodine intake. Enhanced autoimmunity can cause hypothyroidism which is iodine-induced. Finally, it could be speculated that a high or excessive iodine intake may lead to impaired thyroid function due to increased apoptosis of thyroid follicular cells as found in-vitro systems [20].

Gender: Hypothyroidism affects women than men. Study shows that one in eight women may develop thyroid problems, especially hypothyroidism (after menopause) during their lifetime. Thyroid problems affect menstruation, fertility and cause problems related to pregnancy and its outcome [23].

Smoking: Withdrawal from smoking is a risk for the development of hypothyroidism. Withdrawal from smoking causes increase in the level of thyroid antibodies. Tobacco smoking causes variation in thyroid autoimmunity. Smoke has a role to play in certain autoimmune disease as it triggers the development of auto antibodies and act on pathogenic mechanism. It may be related with an imbalance of the immune system [24].

Pesticides: Man made chemicals including pesticides have to be considered as endocrine disruptors. They are interfering in the oestrogen, androgen, thyroid and steroid pathways. Many pesticides are endocrine disrupting chemicals and are capable of interfering the action of natural hormones even at low dose. Evidences point that the pesticide may act as thyroid disruptors and it affects Hypothalamic-Pituitary-Thyroid axis at various levels: may be at central regulation and/or iodine uptake and/or production and distribution of thyroid hormones, or binding of thyroid hormones to membrane transporters or receptors [25].

Medicines: Medicines that are known to suppress the thyroid activity are lithium, amiodarone (inhibition of T3, T4 secretion), interferon, interleukin-2 (thyroiditis), metyrapone (TSH elevation) etc., [26].

Use of plastics: BPA is used to manufacture polycarbonate plastic and epoxy resins. BPA is used to make baby bottles, food package. BPA is known to disrupt endocrine function. There is possibility that BPA acts directly on the thyroid gland, since urinary BPA concentrations were inversely associated with level of thyroid volume in children [27].

Iodine: Iodine is an essential mineral in the formation of Thyroid hormones. It has to be supplied to the body from the foods one eats. A healthy adult has 15-20 mg of iodine in the body and 70-80% of it is seen in thyroid gland. The iodine deficiency is measured through the median urinary iodine concentration. For a non pregnant human being if the concentration is below 100 µg/L, it is considered as deficient. Studies suggested that iodine excess cause thyroid autoimmunity [28,29].

Autoimmunity: Majority of hypothyroidism is caused by autoimmunity. Autoimmunity causes a spectrum of disorders which is caused by inflammation of organs. There is the production of antibodies against self-structures and aggravated cytotoxic action of T cells. Autoimmune thyroid diseases cause the occurrence of anti-Thyroid Peroxidase (TPO), antithyroid-Stimulating Hormone Receptor (TSHR) antibodies and anti-Thyroglobulin (Tg) [30].

Advancing age: Hypothyroidism is more common in advancing age than younger age, especially among older women. Additionally, the incidence of hypothyroidism steadily increases with advancing age. Symptoms of thyroid disorders are very similar to symptoms of the aging process. So, it is very crucial to advance the means of diagnosis thyroid diseases like overt and subclinical hypothyroidism in elderly people [31].

Contaminated water: The quality of water affects thyroid health. Water when contaminated with chemicals, metals, toxins can affect the thyroid gland adversely. The other contaminants can be fluoride, chlorine, bromide, perchlorate, BPA, nitrates, lead. Tap water which contains herbicides, pesticides and other heavy metals are linked loosely to thyroid related issues [32].

Flouride: Flouride inhibits sodium iodine symporter and cause impaired absorption of iodine and iodine concentrating ability. Chronic flouride exposure during infancy may influence iodine status in long run and also health outcomes in adulthood. The study strongly suggests that flouride ingestion contribute to pathological states of thyroid gland [33].

A case control was done to identify the impact of drinking water fluoride on human thyroid hormones in Iran. The purpose of the study was to determine the correlation between thyroid hormones and the presence of fluoride in drinking water. A 198 participants with hypothyroidism were taken as cases and 213 participants with no hypothyroidism were taken as control. The main findings of the study were that TSH value was higher with higher fluoride concentration in the drinking water. The independent variables associated with hypothyroidism were gender (OR:2.5, CI:95%:1.6-3.9), Family History of thyroid disease (OR:2.7, CI:95%:1.6-4.6), Exercise (OR:5.34, CI:95%:3.2-9), Diabetes Mellitus (OR:3.7, CI:95%:1.7-8), Hypertension (OR:3.2, CI:95%:1.3-8.2) amount of water consumed per day (OR: 4, CI:95%:1.2-14). The multiple logistic regression models for factors affecting hypothyroidism show the following factors ($p < 0.2$). Gender, Family History of thyroid disease, educational and job status, quantity of drinking water, exercise, tobacco use, living place, disease history (hyperlipidemia, DM, Hypertension, polycystic, psychiatric conditions and depression) are identified in this study [34].

Another case control study with title prevalence and association of hypothyroidism in Indian patients with Type 2 Diabetes Mellitus was undertaken by Indian Institute of Diabetes, Thiruvanthapuram. Total 1152 patients were included in the study. The prevalence of hypothyroidism was 9.83%. Hypothyroidism was associated with female gender, hypertension, dyslipidemia, obesity, duration of Diabetes more than two years, and anaemia [35]. The present review included 14 studies and all the studies have met inclusion criteria completely. The systematic reviews which were included in the present review scored low when assessed for risk of bias. So, it can be concluded that the present systematic review included studies with minimum risk.

Limitation(s)

The major limitations of the review are related to the selection of articles. Only systematic reviews and review articles have been included in the review. Further, only 14 studies have met the inclusion criteria and have been included in the review. It sounds a small number.

CONCLUSION(S)

The incidence of thyroid disorders in India is high, and is not adequately controlled in the country presently. In India, patients with hypothyroidism are often undetected and untreated. Hypothyroidism is easy to detect and it is easy to treat and it impairs the work performance and productivity of people. The present systematic review tried to explore the various contributing factors of hypothyroidism. The present systematic review identified some new factors which have not been highlighted so far, like influence of fluoride, contaminated water, unregulated use of pesticides, and impact of plastics on thyroid functioning. Case control studies and randomised controlled trials pertaining to these factors can be conducted in future, so that additional factors can be explored with evidences.

REFERENCES

- [1] Nayak CN, Roy S, Chopra P. Pathology of Diseases. Jaypee Brothers Medical Publishers: New Delhi. 2000;441-447.
- [2] Mohan H. Text Book of Pathology. Jaypee Brothers Medical Publishers: New Delhi. 2010;801-814.
- [3] DTE staff. DTW 2018 sep21. Available from file://20review/1%20in%2010%20Indians%20have%20hypothyroidism.html.
- [4] Bagcchi S. Hypothyroidism in India—more to be done. *Lancet Diabetes Endocrinol.* 2014;2(10):778.
- [5] Panday CS, Yadav K, Srivastava R, Panday R, Karmarkar MG. Iodine Deficiency Disorder (IDD) Control in India. *Indian Journal of Medical Research.* 2013;138(3):418-33.
- [6] Aromataris E, Munn Z. JBI manual for evidence synthesis. JBI. 2020. Available from: <https://synthesismanual.jbi.global>. <https://doi.org/10.46658/JBIMES-20-01>.
- [7] Chaithanya NCSK, Karunakar P, Allam NSJ, Priya MH. Systematic Analysis on possibility of water fluoridation causing hypothyroidism. *Systematic Review.* 2018;29(3):358-63.
- [8] Ankim Y, Park YJ. Prevalence and risk factors of subclinical thyroid disease. *Endocrinology and metabolism.* 2014;29(1):20-29.
- [9] Vestergaard P. Smoking and thyroid disorders- a Meta-analysis. *Eur J Endocrinol.* 2002;146(2):153-61.
- [10] Yuan J, Sun C, Jiang S, Lu Y, Zhang Y, Gao XH, et al. The prevalence of thyroid disorders in patients with vitiligo- a systematic review and meta-analysis. *Front Endocrinol.* 2018;9:803.
- [11] Ning Y, Cheng YJ, Liu LJ, Sara JD, Cao ZY, Zheng WP, et al. What is the association of hypothyroidism with risks of cardiovascular events and mortality- A systematic review and Meta analysis. *BMC Med.* 2017;15:21.
- [12] Mathur R. Hypothyroidism symptoms, diet, natural and medical treatments, and tests. Available from: <https://www.medicinenet.com/hypothyroidism/article.htm>.
- [13] Wartofsky L. Hypothyroidism-underactive thyroid. Available from: <https://www.niddk.nih.gov/health-information/endocrine-diseases/hypothyroidism>.
- [14] Editorial. American Thyroid Association. Available from: <https://www.thyroid.org/hypothyroidism/>.
- [15] McIntosh J. What is hypothyroidism? Available from: <https://www.medicalnewstoday.com/articles/163729.php>.
- [16] American Thyroid Association. Hypothyroidism- A booklet for patients and their families (Web Booklet).
- [17] Kharratian D. The Effect of Plastic Products on Autoimmune Disease and Thyroid Function: Stop Using Plastic Coffee Lids!. *Dr K.News.* Available from: <https://drknews.com/effect-plastic-products-autoimmune-disease-thyroid-function-stop-using-plastic-coffee-lids/>.
- [18] Editorial. National Health System. Causes-Underactive thyroid (hypothyroidism) Available from: <https://www.nhs.uk/conditions/underactive-thyroid-hypothyroidism/causes/>.
- [19] Ferrari SM, Fallahi P, Antonelli A, Benvenega S. Environmental issues in thyroid diseases. *Front Endocrinol.* 2017;8:50.
- [20] Pederson IB, Laurberg P, Knudsen N, Jorgensen T, Perrild H, Ovesen L, et al. An increased incidence of overt Hypothyroidism after Iodine fortification of salt in Denmark: A prospective population study. *J Clin Endocrinol Metab.* 2007;92(8):3122-27.
- [21] Gorstein JL, Bagriansky J, Elizabeth N, Pearce, Kupka R, Zimmermen MB. Estimating the Health and Economic Benefits of Universal Salt Iodisation Programme to correct Iodine Deficiency Disorder. *Thyroid.* 2020;30(12).
- [22] National Iodine Deficiency Disorder Control Programme. Available from <https://nhm.gov.in/>.
- [23] Castello R, Caputo M. Thyroid disease and gender. *Ital J Gender-Specific Med.* 2019;5(3):136-141.
- [24] Gutaj NS, Gutaj P, Sowinski J, Ozegowska EW, Czarnywojtek A, Brazert J, et al. Influence of cigarette smoking on throid gland- an update. *Endokrynol Pol.* 2014;65(1):54-62.
- [25] Leemans M, Couderq S, Demeneix B, Fini JB. pesticides with potential thyroid hormone- disrupting effects: A review of recent data. *Front Endocrinol.* 2019.
- [26] Haugen BR. Drugs that suppress TSH or cause central hypothyroidism. *Best Pract Res Clin Endocrinol Metab.* 2009;23(6):793-800.
- [27] Kim MJ, Park YJ. Bisphenols and thyroid hormones. *Endocrinol Metab (Seoul).* 2019;34(4):340-48.
- [28] Chung HR. Iodine and thyroid function. *Ann Paediatr Endocrinol Metab.* 2014;19(10):08-12.
- [29] Teti C, Panciroli MP, Nazzari E, Pesce G, Mariotti S, Oliveri A, et al. Iodoprophylaxis and Thyroid Auto Immunity- an update. *Immunologic Research.* 2021;69:129-38.
- [30] Franco JS, Amaya JA, Anaya JM. Thyroid disease and auto immune diseases. Auto-immunity. El Rosario University Press: Bogota. 2013.
- [31] Kim MI. Hypothyroidism in older adults. *Endotext.* July 2020. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK279005/>.
- [32] Gonskioroski A, Mourikes VE, Flaws JA. Endocrine disruptors in water and their effect on the reproductive system. *Int J Mol Sci.* 2020;21(6):1929.
- [33] Waugh DT. Fluoride Exposure Induces Inhibition of Sodium/Iodide Symporter (NIS) contributing to impaired iodine absorption and iodine deficiency: Molecular mechanism of inhibition and implication for public health. *Int J Environ Res Public Health.* 2019;16(6):1086.
- [34] Kheradpisheh Z, Mirzaei M, Mahvi AH, Mokhtari M, Azizi R, Fallahzadeh H, et al. Impact of drinking water fluoride on human thyroid hormones: A case control study. *Scientific Reports.* 2018;8:2674.
- [35] Nair A, Jayakumari C, Jabbar PK, Jayakumar RV, Raizada N, Gopi A, et al. Prevalence and association of Hypothyroidism in Indian patients with Type 2 Diabetes Mellitus. *J Thyroid Res.* 2018;2018:5386129.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Community Health Nursing, College of Nursing, Thalassery, Kannur, Kerala, India.
2. Principal, College of Nursing, Yenepoya Deemed to be University, Mangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Salina Sunil,
Lakshminand, Panoor, Kannur District-670692, Kerala, India.
E-mail: salina.surabhi@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jun 18, 2021
- Manual Googling: Nov 09, 2021
- iThenticate Software: Dec 30, 2021 (20%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Jun 17, 2021**

Date of Peer Review: **Sep 13, 2021**

Date of Acceptance: **Nov 23, 2021**

Date of Publishing: **Jan 01, 2022**