MERIT RESEARCH JOURNALS
www.meritresearchjournals.org

Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-323X) Vol. 8(9) pp. 529-536, September, 2020
Available online http://www.meritresearchjournals.org/mms/index.htm

DOI: 10.5281/zenodo.4060241

Original Research Article

Relationship between the Thyroid Cell Dysfunction and Vitamin D Deficiency

Dr. Itedal Abdelraheem Mohamed Ahmed

Najran University- Faculty of Medicine, Department of Anatomy

E-mail: itedalanatomy@gmail.com

Abstract

Little is known about the role of vitamin D deficiency in thyroid cell dysfunction among patients with common types of thyroid disorder. This qualitative, descriptive cross-sectional study analyzed frequent causes of and risk factors for thyroid disorders associated with thyroid cell dysfunction among patients in hospitals in Najran, Saudi Arabia, from December 2018 to December 2019. Seventy-four patients were identified with thyroid disorders, including 51 (68.9%) with hypothyroidism, 19 (25.7%) with hyperthyroidism and four (5.4%) with thyroid cancer. Hyperthyroidism correlated with psychological stress (r = 0.233, P = 0.046) and high doses of thyroid hormones (r = 0.284, P = 0.014), but not with unconsciousness due to trauma (r = 0.093, P = 0.432), thyroiditis (r = 0.047, P = 0.693) or vitamin D deficiency (r = -0.197, P = 0.092). Logistic binary regression analysis showed that high-dose thyroid hormone was independently associated with hyperthyroidism, as shown by the equation, Log (Hyperthyroidism) = -21.203-+ 22.377 high doses of thyroid hormone. Hypothyroidism correlated with vitamin D deficiency (r =0 .279, P = 0.016), but not with partial thyroidectomy (r = -0.010, P = 0.933) exposure of the head and neck to radiation (r = 0.079, P = 0.506), thyroiditis (r = 0.020, P = 0.868), or lack of iodine in food (r = 0.064, P = 0.585). Analysis showed that Logit (Hypothyroidism) = -1.308+ 1.234 vitamin D deficiency +1.802 thyroiditis. Hypothyroidism was the most frequent type of thyroid disorder in these patients and was significantly correlated with vitamin D deficiency, suggesting that vitamin D plays a beneficial role in the management of thyroid disorders. Hyperthyroidism correlated with thyroiditis and high doses of thyroid hormone.

Keywords: Cell and Molecular Biology, Hyperthyroidism, Hypothyroidism, Thyroid anatomy, Thyroid histology, Vitamin D

INTRODUCTION

The aim of the present study focused on the role of vitamin D in thyroid diseases, including autoimmune thyroid diseases and thyroid cancers. The purpose of this study was to determine the most common types of thyroid disorders and their association with vitamin D deficiency, thereby assessing the role of vitamin D deficiency in thyroid cell dysfunction.

The thyroid is an endocrine gland that plays an important role in metabolism and in controlling growth and development. The butterfly-shaped thyroid gland is composed of two lobes separated by an isthmus and is situated in the anterior part of the neck, between the C5 and T1 vertebrae. The thyroid gland stores iodine, which it uses in the synthesis of the thyroid hormones triiodothyronine (T3) and thyroxine (T4), which are secreted into the blood (Schmidt et al., 2010). Thyroid hormone synthesis is controlled by thyroid-stimulating hormone (TSH), which is released by the cells of the pars distalis of the pituitary gland, whereas the pituitary gland is regulated by thyrotropin-releasing hormone, which is produced by the hypothalamus.

The morbidities associated with untreated thyroid disease (Diamond et al., 1994; Flynn et al., 2004) can be reduced by effective treatment. The incidence and prevalence of thyroid diseases, and especially hyperthyroidism, have been reported in European populations. The incidence of primary hypothyroidism was found to vary from 0.14 to 3.53 patients per 1000 people per year (Díez et al., 2003), and the prevalence of hypothyroidism has been reported to vary from 1.4% in Denmark to 4.8% in Norway (Bülow Pedersen et al., 2002; Brownlie and Wells, 1990; Berglund et al., 1996). The incidence of hyperthyroidism has been found to range from 0.26 to 0.93 per 1000 people per year in Europe (Díez et al., 2003; Berglund et al., 1996; Lundgren and Borup Christensen, 1990) but is more common in areas of iodine deficiency. Although there are apparent geographical variations in the incidence of thyroid disorders, few studies have assessed the changing incidence of thyroid diseases over time within a single center. Studies to date have reported contradictory results, with some showing a decreasing incidence and others showing an increasing incidence of hyperthyroidism over time (Lundgren and Borup Christensen, 1990). Previous study reported the prevalence of thyroid diseases in Tayside, Scotland (Díez et al., 2003), and are now able to report the annual incidence and prevalence of different thyroid conditions over eight years from 1994 to 2001.

Patients with hypothyroidism are deficient in vitamin D and calcium, deficiencies closely related to the degree and severity of hypothyroidism. Low vitamin D concentrations have been reported associated with autoimmune thyroid diseases such as Hashimoto's thyroiditis and Graves' disease, and impaired vitamin D signaling has been reported in patients with thyroid cancers (Kim, 2017). Among patients with hypothyroidism, the occurrence of vitamin D insufficiency tended to be higher in patients with overt hypothyroidism (47/50, 94%) or subclinical (44/45, 98%) hypothyroidism than in patients with euthyroidism (57/66, 86%), although the differences were not statistically significant (Tamer et al., 2011). These findings suggest the importance of screening vitamin D and blood calcium levels in patients with thyroid diseases and the necessity of vitamin D supplementation in patients with hypothyroidism (Mackawy et al., 2013).

MATERIALS AND METHODS

The qualitative, descriptive cross-sectional study analyzed frequent causes of and risk factors for thyroid disorders associated with thyroid cell dysfunction among patients in hospitals in Najran, Saudi Arabia, from December 2018 to December 2019. The sampling technique was based on probability proportionate to the size of the population. Patients were administered questionnaires assessing demographic and clinical factors, including those previously identified as being associated with thyroid disorders. Doctors and staff nurses entered the completed questionnaires, daily into a specially designed SPSS access database on duty in the clinic.

Statistical Analysis

The descriptive frequency was determined, and logistic binary regression analysis and correlation probabilities assessed. A P-value, $p < 0.05$ (2-sided) was considered to indicate statistical significance. Correlations between variables were assessed by measuring Pearson correlation coefficients (r), with r-values<0.3, 0.3–0.5, 0.5–0.7, and >0.7 indicating very weak, weak, moderate, and strong correlations, respectively, and direction assessed as positive or negative (Bewick et al., 2013). All statistical analyses were performed using IBM SPSS statistics for Windows, Version 25.00 (Armonk, NY: IBM Corp.), and Microsoft Excel Software, with a two-sided p-value <0.05 indicating statistical significance (Table 1).

RESULTS

Seventy-four patients were identified with thyroid disorders during the study period, including 51 (68.9%) with hypothyroidism, 19 (25.7%) with hyperthyroidism, and four (5.4%) with thyroid cancer (Figure 1).

Hyperthyroidism correlated significantly with psychological stress (r = 0.233, P = 0.046) and high doses of thyroid hormones (r = 0.284, P = 0.014), but not with unconsciousness due to trauma (r = 0.093, P = 0.432), thyroiditis (r = 0.047, P = 0.693) or vitamin D deficiency (r = -0.197, P = 0.092) (Figure 2).

Logistic binary regression analysis showed that high dose thyroid hormone was independently associated with hyperthyroidism, as shown by the equation, Log (Hyperthyroidism) = -21.203±22.377 *high doses of thyroid hormone (Figure 3).

Logistic binary regression analysis also showed that psychological stress had a score 4.834 (P = 0.028), which was statistically significant, whereas vitamin D deficiency had a score of 1.494 (P = 0.222), unconsciousness due to trauma had a score of 0.794 (P = 0.373), and thyroiditis had a score of 0.415 (P = 0.519) (Figure 4).

Hypothyroidism correlated with vitamin D deficiency (r =0 .279, P = 0.016), but not with partial thyroidectomy (r = -0.010, P = 0.933) exposure of the head and neck to radiation (r = 0.079, P = 0.506), thyroiditis (r = 0.020, P = 0.868), or lack of iodine in food (r = 0.064, P = 0.585) (Figure 5).

Analysis showed that Logit (Hypothyroidism) = -1.308+ 1.234 vitamin D deficiency +1.802 thyroiditis (Figure 6).

Table 1. Guidelines for coefficients (r) between variables

	Coefficient, r	
Strength of Association	**Positive**	**Negative**
Very weak	r < 0.3	r <-0.3
Weak	0.3 < r <0.5	- 0.3 < r < -0.5
Moderate	0.5 < r < 0.7	- 0.5 < r <-0.7
Strong	r > 0.7	r >-0.7

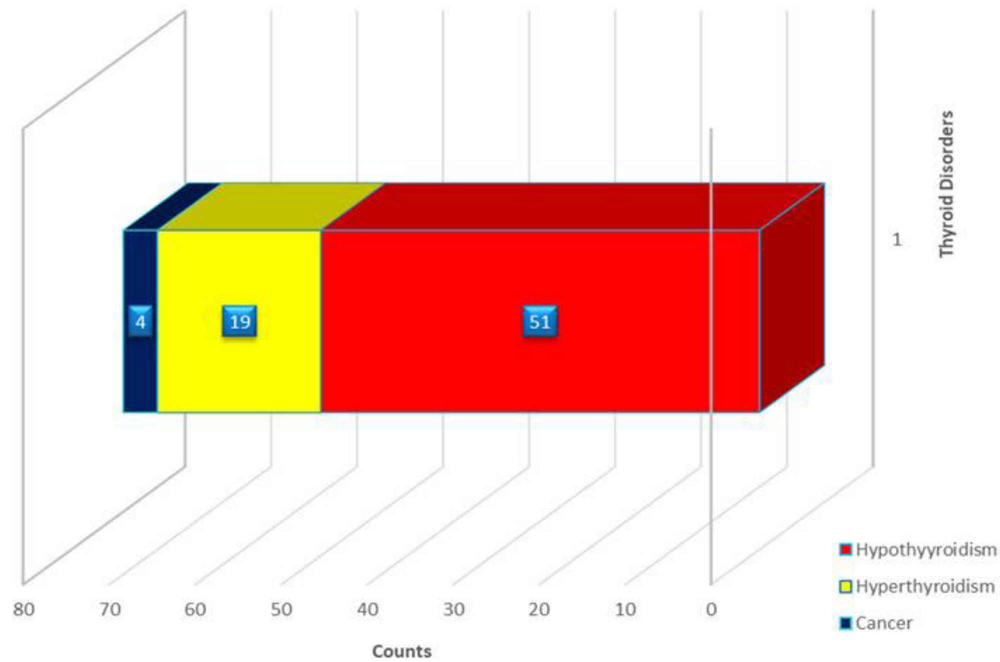

Figure 1. Frequencies of different types of thyroid disorders in the study population

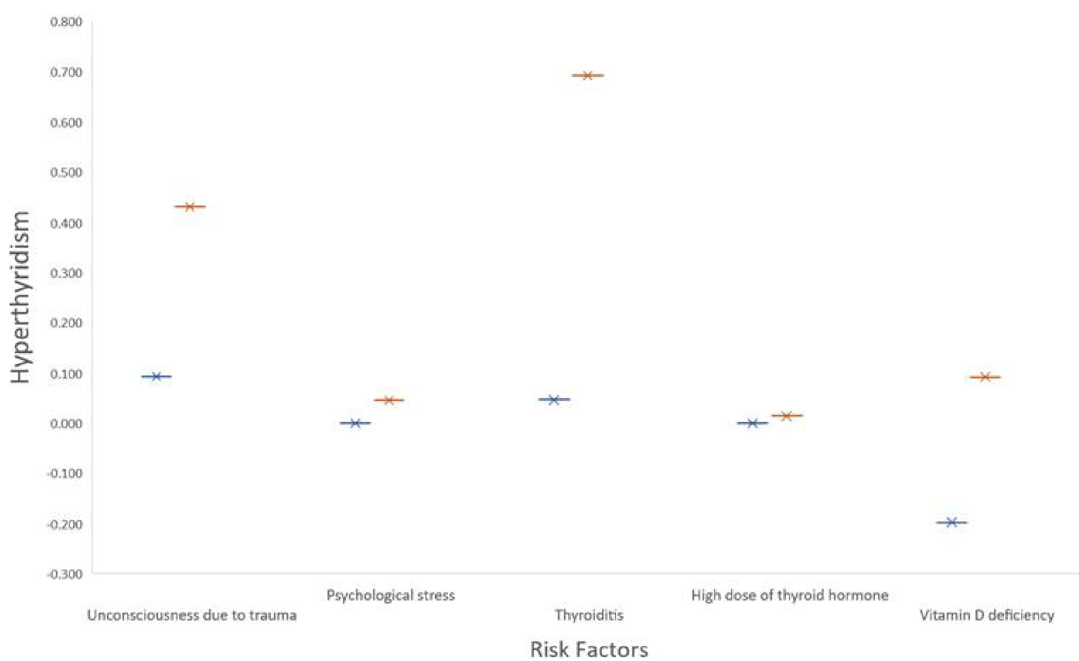

Figure 2. Correlations between hyperthyroidism and putative risk factors

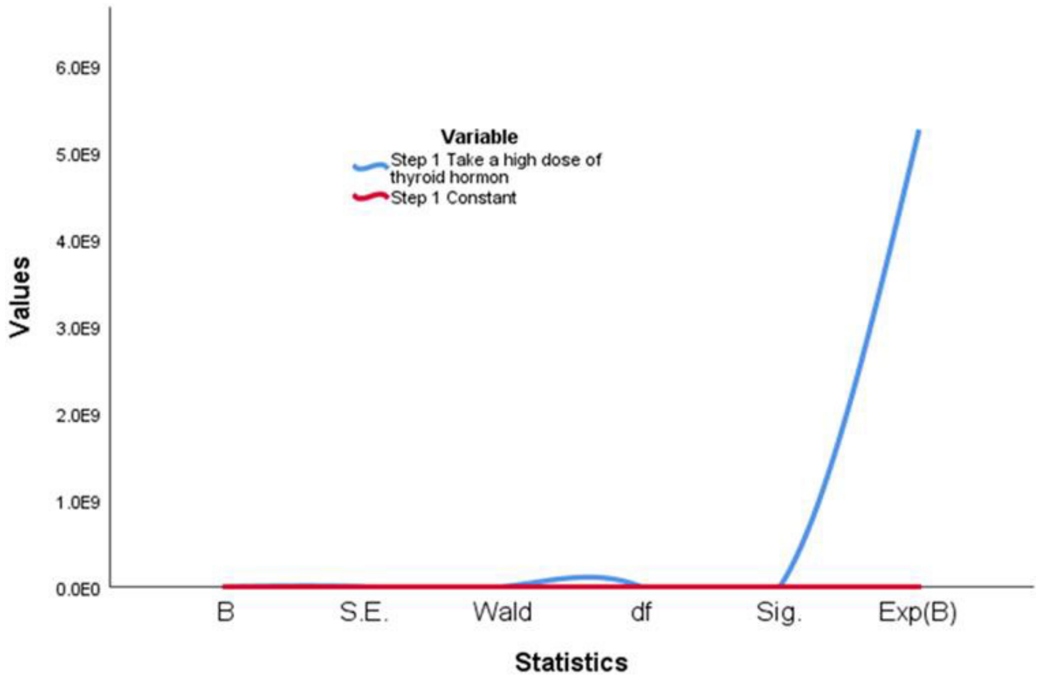

Figure 3. Variables in the equation significantly associated with hyperthyroidism. Abbreviations: B, constant; S.E., standard error; Wald, test methods given by SPSS statistics to standard regression analysis; df, standard deviation; Sig, significant; Exp. (B), odds ratio to the power B

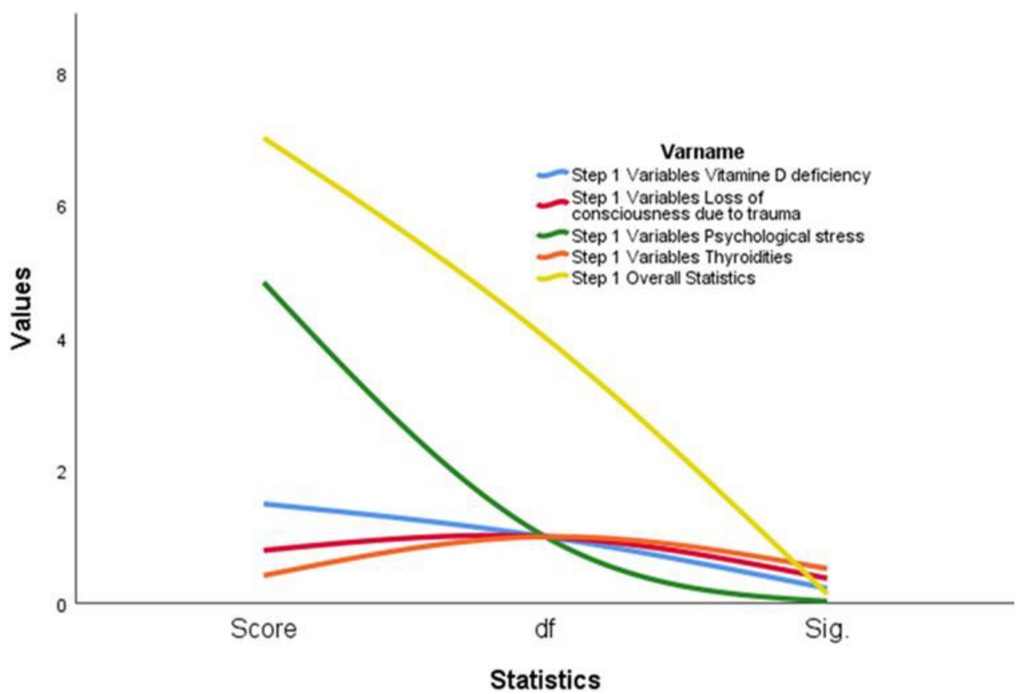

Figure 4. Variables not in the equation and their association with hyperthyroidism. Abbreviations: df, standard deviation; Sig, significant

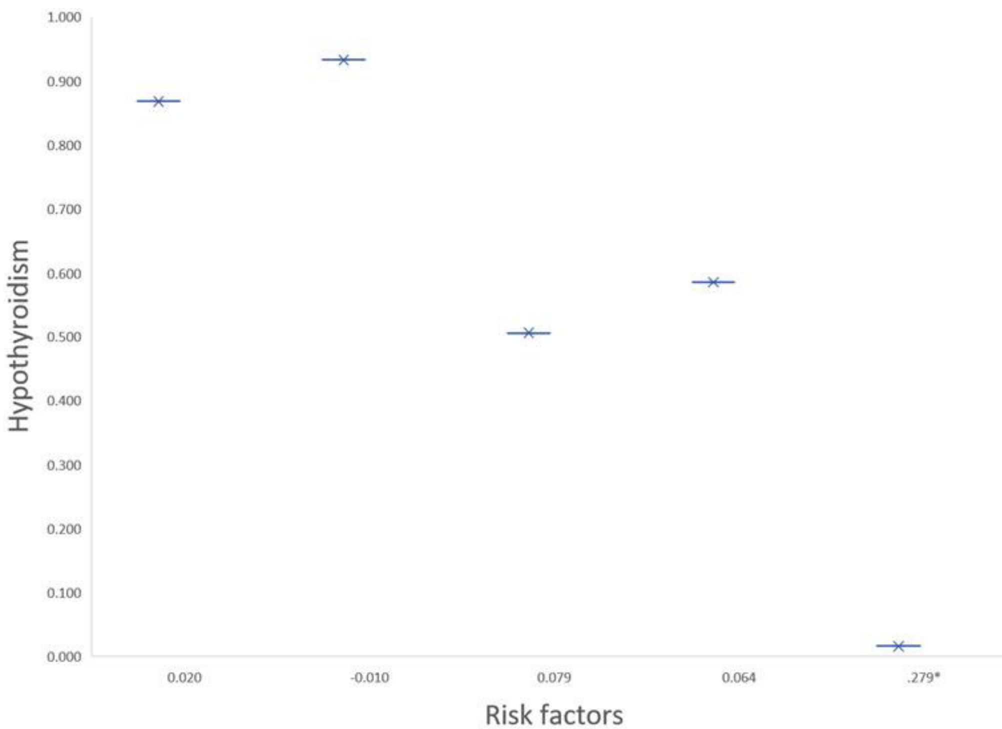

Figure 5. Correlations between hypothyroidism and putative risk factors. *Significant correlation at the 0.05-level (2-tailed)

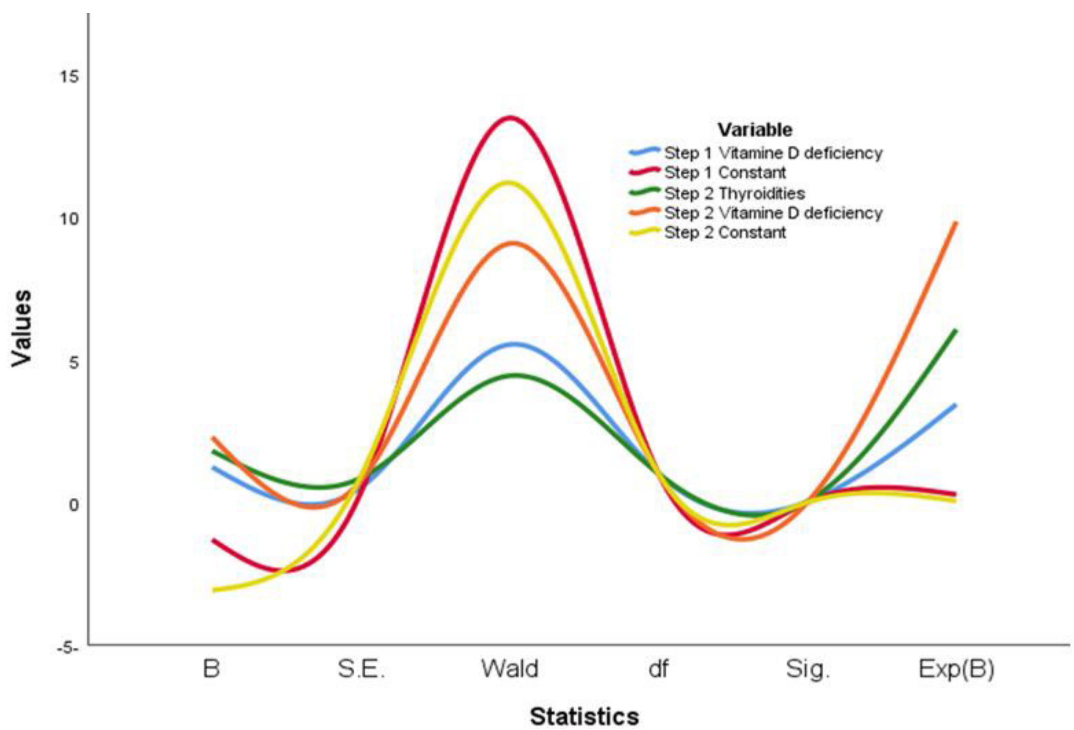

Figure 6. Variables in the equation significantly associated with hypothyroidism. Abbreviations: B, constant; S.E., standard error; Wald, test methods given by SPSS statistics to standard regression analysis; df. standard deviation; Sig, significant; Exp. (B), odds ratio and to the power B.

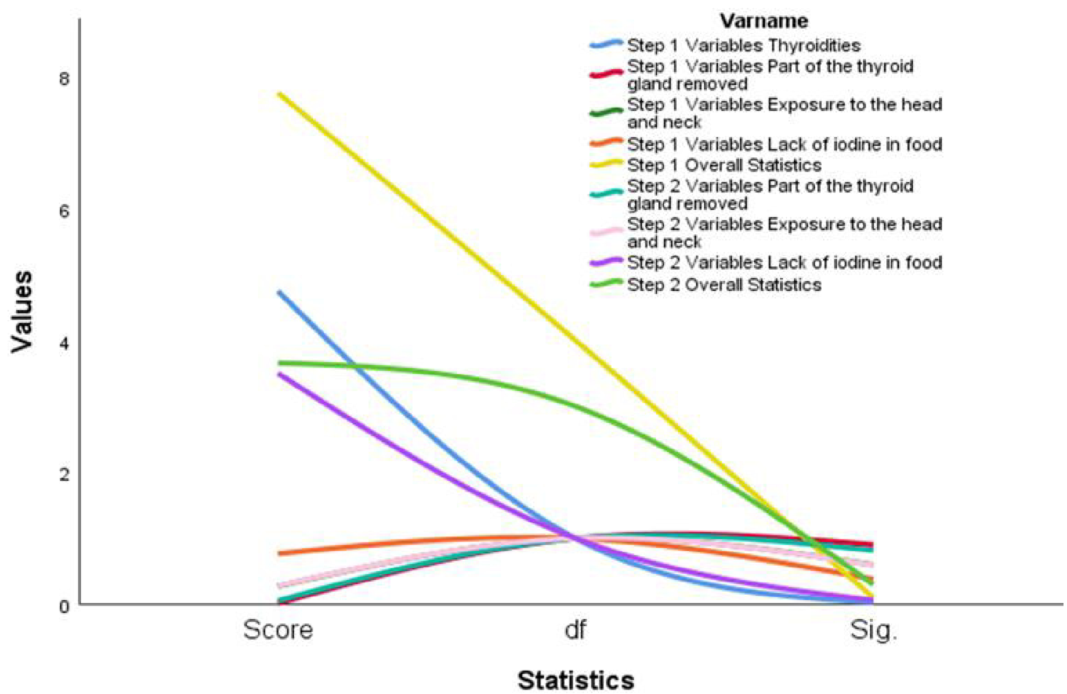

Figure 7. Variables not in the equation and their association with hypothyroidism. Abbreviations: df, standard deviation; Sig, significant

Table 2. Showing the distribution of risk factors of thyroid cell dysfunction among the study population

Risk factors	Thyroid cell dysfunction			
	Simple Frequency		Relative frequency %	
	Yes	No	Yes	No
Vitamin D deficiency	47	27	63.5	36.5
Thyroiditis	17	57	23	77
Thyroidectomy	3	71	4.1	95.9
Radiation exposure to the head and neck	1	73	1.4	98.6
Lack of iodine in food	5	69	6.8	93.2
Unconsciousness due to trauma	2	72	2.7	97.3
Psychological stress	7	67	9.5	90.5
Take a high dose of thyroid hormone	2	72	2.7	97.3
Total patient with thyroid disorder	74 (100 %)			

The first step of logistic binary regression analysis also showed that thyroiditis had a score pf 4.748 (P = 0.029), which was statistically significant. Whereas partial thyroidectomy had a score of 0.015 (P = 0.901), radiological exposure of the head and neck had a score of 0.276 (P = 0.599). In addition, lack of iodine in food had a score of 0.767 (P = 0.381) (Figure 7).The second step of logistic binary regression analysis showed that partial thyroidectomy, radiological exposure of the head and neck, and lack of iodine in food had scores of 0.054 (P = 0.817), 0.282 (P = 0.595), and 3.503 (P = 0.061), respectively.

We examined the relationship between risk factors, specifically vitamin D deficiency and thyroid cell dysfunction using percent frequencies. We found 47 thyroid disorder patients with vitamin D deficiency (63.5%) through descriptive frequency analysis (Table 2).

DISCUSSION

Thyroid cell dysfunction can affect the entire body. Overproduction of thyroid hormone is called hyperthyroidism, whereas the underproduction of thyroid hormone is called hypothyroidism. Of the patients with thyroid dysfunction assessed in this study, most had hypothyroidism, in agreement with previous studies (Berglund et al., 1996). Thyroid cells in these patients were destroyed structurally and functionally, making them unable to produce sufficient hormones for vital processes in the body.

Thyroid tissue is composed of two types of cells, thyroid follicular cells (TFCs) and parafollicular cells (C-cells) (Young et al., 2013). The C-cells, which are situated between the follicular epithelial cells and their basement membranes, produce the hormone calcitonin, which is responsible for regulating the level of calcium in the blood (Matias-Guiu and De Lellis, 2014; Erickson, 2014). C-cells have been associated with medullary thyroid carcinoma (MTC), and MTCs are thought to originate from neuroectodermal cells (Williams, 1966). C-cell hyperplasia, generally defined as an increase in the number of C-cells within the follicles of the thyroid gland, has been associated with familial MTC and is regarded as a precursor of MTC (Wolfe et al., 1973; Scognamiglio, 2017).

TFCs primarily regulate thyroid functions, such as the secretion and production of thyroid hormones, including T3 and T4. A monolayer of TFCs regulates follicles in honey-like structures that produce thyroglobulin (TG), which is modified with iodine to produce thyroid hormones (Young et al., 2013). The process underlying the secretion of T3 and T4 consists of several complex steps: (1) synthesis of TG, a large molecular weight glycoprotein, in follicular epithelial cells. (2) Release of TG into the follicular lumen. (3) Iodination of the tyrosine residues of TG. (4) Reabsorption of TG from the follicular lumen by follicular epithelial cells; (5) hydrolysis of TG to produce T3 and T4; and (6) secretion of T3 and T4 by follicular epithelial cells into the connective tissue space (Fujita, 1975).

Various disorders can cause thyroid cells to malfunction. Hypothyroidism results from a deficiency in the synthesis and release of thyroid hormones (Delange, 1994). Iodine deficiency is the most common cause of hypothyroidism. Lack of iodine can result in an enlarged thyroid gland, as well as other symptoms, such as heart problems, pregnancy-related problems, and weight gain (Delange, 1994). In areas of iodine sufficiency, the most common cause of hypothyroidism is Hashimoto's thyroiditis, an autoimmune disease (Caturegli et al., 2014). Hyperthyroidism, which results from the synthesis of excess thyroid hormones, is most often due to the autoimmune disorder Graves' disease (Streetman and Khanderia, 2003).

Autoimmune thyroid disease (AITD) results from a combination of genetic, environmental, and constitutional factors. For example, the frequency of AITD has been shown higher in family members of patients with autoimmune hypothyroidism and Graves' disease than in the general population (Weetman and McGregor, 1994). In Europe, the prevalence of Graves' disease increases with national iodine intake programs. Iodine increases the antigenicity of TG, thereby exacerbating experimental AITD in animals. High iodine concentrations may damage thyrocytes and enhance disease progression in a dose-dependent manner (Rose et al., 2002). Congenital rubella syndrome has been associated with AITD, and Yersinia infection has been shown to correlate with Graves' disease (Tomer and Davies, 1993). Major life events may be associated with Graves' disease, with stress playing a causal role in the autoimmune process (Swain et al., 2005). Other factors associated with thyroid dysfunction include valence, smoking, age, and body mass index (Veltri and Poppe, 2018).

Destruction of thyroid follicular cells has been shown to depend on the chronicity of Hashimoto's thyroiditis (Swain et al., 2005). Although thyroid activity is increased under conditions of severe iodine deficiency, thereby maximizing iodine uptake (Zimmermann and Boelaert, 2015) and recycling, iodine concentrations remain too low to enable thyroid hormone production. Thus, severe iodine deficiency can cause goiter and hypothyroidism.

Hyperthyroidism in this study was significantly associated with high doses of exogenous thyroid hormones. In contrast, the most frequent causes of hypothyroidism was vitamin D deficiency, which was significantly associated with the inability of thyroid cells to secrete sufficient thyroxine for vital processes in the body. Vitamin D supplementation may play a beneficial role in the management of thyroid cell dysfunction (Lundgren and Borup Christensen, 1990; Kim, 2017). Previous studies have also shown that vitamin D insufficiency tended to be higher in patients with overt hypothyroidism (Tamer et al., 2011). Vitamin D deficiency in patients with hypothyroidism is frequently accompanied by hypocalcemia, which is closely related to the degree and severity of hypothyroidism. These findings suggest that vitamin D and blood calcium levels be measured in all patients with thyroid disorders and that vitamin D supplements should be administered to hypothyroid patients (Mackawy et al., 2013).

The most common type of thyroiditis, defined as inflammation of the thyroid gland, is Hashimoto's disease, an autoimmune disorder. In this disease, white blood cells attack a patient's thyroid cells, inducing the pituitary gland to release TSH, which stimulates the thyroid gland to produce more thyroid hormone. This pressure on the thyroid gland can cause its enlargement (goiter). The destruction of thyroid follicular cells in these patients is dependent on the chronicity of Hashimoto's thyroiditis (Bewick et al., 2013).

Limitation of the study

An examination of thyroid hormones was difficult because many did not respond regarding patients with thyroid disorder. Another limitation was that we were not able carry out a laboratory measurement of vitamin D in all patients with thyroid disorders, which led to a smaller population than required for this study (which was 384 participants, according to the study population and the sample size).

CONCLUSION

Hypothyroidism was the most frequent type of thyroid disorder in these patients and was significantly correlated with vitamin D deficiency, suggesting that vitamin D plays a beneficial role in mitigating thyroid cell dysfunction. While our findings seem to confirm the role of vitamin D in causing the hypothyroidism, the association is not fully vetted. Hyperthyroidisms correlated with thyroiditis and high doses of thyroid hormone. Thyroid cell dysfunction caused by medications should be considered when thyroid function test results are inconsistent with the clinical protocol or when the patient is taking a drug known to impair thyroid function. A distinction must be made between false abnormalities in thyroid function tests and true thyroid impairment. Certain medications or agents can cause either or both of these abnormalities. Therefore, an understanding of their potential effects on the thyroid gland will help the physician manage the patient appropriately.

ACKNOWLEDGMENTS

The authors thank the staff of Najran University Hospital and Scientific Research and Conferences Committee for their invaluable help.

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