Volume :2/ Issue : 2/ Jul –Dec 2013

ORIGINAL ARTICAL Medical Science

Status of thyroid function in patients with suspected irritable bowel syndrome in Karkuk city A cross-sectional study

Dr. Faisal Gh. Al-Rubaye (PhD; MBChB.)* Dr. Yaldiz Hasan Tahsein(PhD; BSc.) ** Dr. Samar Saad Abdul-Husain (CABM (GIT); MBChB.)***

*Department of Chemistry & Biochemistry, College of Medicine, Al-Nahrain University

**Department of Biochemistry, College of Medicine, Karkuk University.

***Department of Medicine, College of Medicine, Karkuk University

Address for correspondence

Dr. Faisal Gh. Al-Rubaye (PhD; MBChB.) Department of Chemistry & Biochemistry, College of Medicine, Al-Nahrain University Baghdad –Iraq

E-mail: faisal3ghazi@yahoo.com

ABSTRACT

BACKGROUND:

Irritable bowel syndrome (IBS) is a common public health The condition is characterized by a scarcity of biological markers; thus, diagnostic definitions and classifications have relied to a large extent on symptoms, gastrointestinal manifestations of patients with functional abnormalities of the thyroid is not well documented. While thyroid disorder should be considered in the differential diagnosis of patients with IBS symptoms, it is not clear if thyroid disturbances amongst patients with IBS are high enough to warrant routine screening.

OBJECTIVE:

To comparing thyroid function in patients with IBS to that of healthy volunteers undergoing routine colorectal cancer screening.

METHODS:

A cross-sectional study conducted at the Gastroenterology clinic of the Teaching Hospital of Karkuk Medical College between September 2010 and September 2012, there were two study populations enrolled in this study. An IBS group composed of consecutive adult female patients with suspected IBS fulfilled the Rome II criteria for IBS, and the control group consists of women who were scheduled for screening colonoscopy.

Thyroid Function Test (TFT) was done for the two groups that include measurement of thyroid hormones (T3 and T4) together with thyrotropin stimulating hormone (TSH).

RESULTS: disturbance of thyroid function was found among patients with IBS when compared with healthy subjects.

CONCLUSIONS: the convenience of TFTs suggest that their routine use in the diagnostic evaluation of established IBS patients should be recommended in populations at a high risk of thyroid problems.

Key words: Thyroid function, IBS, Colonoscopy**.**

Introduction

Irritable bowel syndrome (IBS) is a common public health problem that affects approximately 12% of adults in the United States and between 10%-12% in other industrial countries.[1,2]

IBS can be classified according to the predominant bowel symptoms: IBS with constipation-predominant features (IBS-C), IBS with diarrhea-predominant features (IBS-D) and IBS with alternating symptoms of diarrhea and constipation (IBS-A).[3] The condition is characterized by a scarcity of biological markers; thus, diagnostic definitions and classifications have relied to a large extent on symptoms, typically distinguished by persistent or recurrent abdominal pain related to defecation and/or chronic disturbance of bowel habits. [3-5]

The true incidence of gastrointestinal manifestations of patients with functional abnormalities of the thyroid is not well documented. Gastrointestinal motor dysfunction, manifested by altered intestinal motility and transit time, has widely been accepted as the leading cause of gastrointestinal symptoms of thyroid disease[6]. Patients with hyperthyroidism can experience frequent bowel movements, diarrhea, even malabsorption with steatorrhea[6-8]. Chronic dyspeptic symptoms such as epigastric pain and fullness, as well as eructation, nausea and vomiting are also frequently seen in these patients. Less commonly, hyperthyroidism has been reported to cause persistent and intractable vomiting[9].

The overall decreased metabolic function seen in patients with hypothyroidism manifests in the GI tract with sluggish intestinal motility, ranging from mild constipation to paralytic ileus and colonic pseudoobstruction[10]. While thyroid disorder should be considered in the differential diagnosis of patients with IBS symptoms, it is not clear if thyroid disturbances amongst patients with IBS is high enough to warrant routine screening. Herein the findings from the first prospective, cross-sectional study comparing thyroid function in patients with IBS to that of healthy volunteers undergoing routine colorectal cancer screening.

Material and Methods

This was a cross-sectional study conducted at the Teaching Hospital of Karkuk Medical College between September 2010 and September 2012.

Subjects:

There were two study populations enrolled in this study. An IBS group composed of consecutive female adult patients with symptoms suggestive of IBS were identified in the Gastroenterology clinic. Patients with suspected IBS fulfilled the Rome II criteria for IBS based on their responses to a questionnaire administered in the clinic. (11)

Patients in the IBS group were referred for a diagnostic evaluation of their IBS symptoms. Patients were excluded from the study if they had been previously diagnosed with co-morbid conditions that could have explained their GI symptoms (e.g. celiac disease, colon cancer, inflammatory bowel disease (IBD), scleroderma, small intestinal bacterial overgrowth, uncontrolled thyroid disease or diabetes). Patients with previous GI or intestinal (large or small bowel) surgery, with the exception of appendectomy or cholecystectomy, were also excluded. Patients reporting symptoms suggestive of organic diseases were excluded from the study also women who were pregnant or breast-feeding or patients who had undergone previous diagnostic testing for their IBS symptoms were excluded from the study. No participants had been previously tested for thyroid function.

The control group consisted of individuals who were scheduled for screening or surveillance colonoscopy, either due to primary care referrals or self-referral. Controls were recruited from the teaching hospital of Karkuk Medical College prior to their colonoscopy. All controls completed the same Rome II GI symptom questionnaire to confirm the absence of IBS symptoms.

Blood samples: five milliliters of random venous blood were withdrawn from each patient, in supine position, without application of tourniquet. Samples were transferred into clean new plane tube, left at room temperature for 15 minutes for clotting, centrifuged at 1800 x g for 10 minutes at 4°C, and the separated serum was transferred into Eppendrof tube and was used for measurement of Thyroid Function Test (TFT) that include measurement of thyroid hormones (T3 and T4) together with thyrotropin stimulating hormone (TSH).

Methods:

TFT was evaluated using autobio diagnostics Thyroid ELISA kits (an autobio group company www.autobio-diagnostics.com).

PRINCIPLE OF THE ASSAY

The quantitative immunoenzymatic determination of TFT (TSH, T3 & T4) is based on the ELISA (Enzyme-linked Immunosorbent Assay) technique. The assay system utilizes two monoclonal antibodies specific for different antigenic determinants of each of the (TSH, T3 & T4). The first antibody is immobilized on the surface of the microtiter wells. The second antibody is conjugated to horseradish peroxidase. The test sample is allowed to react simultaneously with the two antibodies, resulting in the (TSH, T3 & T4) molecules being sandwiched between the solid phase and the enzyme-linked antibodies. After an incubation step, the wells are washed with Washing Solution to remove all unbound material. The immune complex is visualized by adding Tetramethylbenzidine (TMB) substrate which gives a blue reaction product. The intensity of this product is proportional to the concentration of (TSH, T3 & T4) in the specimen. Sulphuric acid is added to stop the reaction. This produces a yellow endpoint colour. Absorbance is read using an ELISA microwell plate reader. The color intensity is directly proportional to the concentration of (TSH, T3 & T4) present in the test sample (instruction manual for autobio diagnostics Thyroid ELISA kits).

Statistical Analysis

statistical analysis was done using Excel system version 2003 and includes descriptive statistics (mean and standard deviation) and inferential statistics (*t-test*) to test the significancy of mean difference. When P-value was less than 0.05, the difference is considered statistically significant, and the difference is considered highly significant when P-value was less than 0.001.

Results

A total of 70 patients with symptoms suggestive of IBS was included in IBS-group, these were compared with 80 apparently healthy subjects who were included in the control-group the clinical criteria for both groups was shown in table 1. TFT: Serum of thyroid hormones was altered in IBS group when compared with the control group in that the level of T3 was significantly elevated [$P < 0.05$] associated with significant reduction in TSH [$P < 0.05$]; however, the level of T4 was not significantly altered between the two groups [$P > 0.05$] As in Table 2.

Discussion

According to the results of the current study, altered thyroid function was found in patients with suspected IBS when compared with healthy volunteers, these findings were in disagreement with the findings of Hamm et., al [12] who fail to modify the criteria for diagnosis of IBS.

The mechanism behind our results was not clear; however, direct hormonal effects or stimulatory actions in the central nervous system have been suggested. Treatment of the thyrotoxicosis with beta blocking agents and anti-thyroid drugs greatly improves these symptoms[13].

The exact biochemical mechanism by which thyroid disorders affect the gastrointestinal system are not fully understood. Changes may be seen on a molecular level with alteration of hormone receptors, dysfunction of the autonomic nervous system and myoelectrical enteric activity, as well as changes on a tissue level in the form of myopathy[14].

Hormonal effects on the GI tract may be a direct result of thyroid hormone, or as a result of synergistic effects of catecholamines. Tenore et al. investigated the effect of thyroxin (T4) on the intestinal chloride/bicarbonate exchange in hypo- and hyperthyroid rats. They found that alterations in intestinal ion exchange, mainly the flux of chloride, led to mucosal effects and resultant diarrhea. These findings were not seen when T4 was added ex vivo to rat ileum, suggesting that the effect on electrolyte transport likely requires systemic factors[15]. Furthermore, the beta-adrenergic antagonist propranolol inhibits intestinal transit in hyperthyroidism, thereby indicating that some of the dysmotility may be mediated through the adrenergic/catecholamine system[16]. Dysfunction of the autonomic nervous system (ANS) may modify the neuro-hormonal milieu, and result in alterations of myoelectric activity. However, there are no clear data regarding the exact mechanisms involved.

Hypothyroidism characteristically results in accumulation of glycosaminoglycans, mostly hyaluronic acid, in interstitial tissues throughout the body. This leads to interstitial edema that is particularly evident in the skin, heart muscle, and skeletal muscle, but also in the gastric smooth muscle. Edema in the gastric muscle may predispose to abnormalities of gastric myoelectric activity and thus the dysmotility seen in hypothyroid patients[17].

Examination of TFTs in patients with an established history of IBS revealed an altered function of thyroid comparable to that

in the general population; this might be attributed to high incidence of thyroid problems in older adults [18].

Thus, the convenience of TFTs suggest that their routine use in the diagnostic evaluation of established IBS patients should be recommended in populations at a high risk of thyroid problems

Table (1): Clinical criteria of women with IBS & Controls (presented as range and mean ± SD).

Group	***IBS-group***	***Control-group***	***p-value***
No	***70***	***80***	
Age / year (Mean + SD)	***45 ± 10.5***	***42 ± 7***	> 0.05
Age range (years)	***18-70***	***29-64***	
BMI (kg/m²) (mean ± SD)	***24.7 ± 3.5***	**24 ± 3**	> 0.05
BMI Range(kg/m²)	***18-30***	***19-30***	

Table (2): Thyroid Function Test (The mean serum T3, T4, TSH) in different women with IBS and controls (presented as mean ± SD).

Variable	**IBS-group**	**Control-group**	**p-value**
serum T3 (IU/L)	1.8 ± 0.8	1 ± 0.2	< 0.05
Serum T4	69 ± 5.8	68 ± 3.4	> 0.05
Serum TSH	2 ± 1	2.6 ± 1.9	< 0.05

The authors declare that they have no conflict of interest.

REFERENCES

1.Drossman DA, Li Z, Andruzzi E, et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. *Dig Dis Sci.* 1993;38(9):1569-80.

2.Mertz HR. Irritable bowel syndrome. *N Engl J Med.* 2003; 349(22): 2136-46. Available at: www.content.nejm.org/cgi/reprint/349/22/2136.pdf. Accessed October 20, 2008.

3.Thompson WG, Dotevall G, Drossman DA, Heaton KW, Kruis W. Irritable bowel syndrome: guidelines for the diagnosis. *Gastroenterol Int.* 1989;2:92-95.

4.Drossman DA, Thompson WG, Talley NJ, Funch-Jensen P, Janssen J, Whitehead WE. Identifications of subgroups of functional gastrointestinal disorders. *Gastroenterol Int.* 1990;3:159-72.

5.Wegener M, Wedmann B, Langhoff T, Schaffstein J, Adamek

6.R. Effect of hyperthyroidism on the transit of a caloric solidliquid meal through the stomach, the small intestine, and the colon in man. *J Clin Endocrinol Metab* 1992; **75:** 745-749.

7.Tinker MB. Discussion of paper by Verbrycke JR. Masked gastrointestinal hyperthyroidism. *JAMA* 1931; **97:** 515-516

8.Karaus M, Wienbeck M, Grussendorf M, Erckenbrecht JF, Strohmeyer G. Intestinal motor activity in experimental hyperthyroidism in conscious dogs. *Gastroenterology* 1989; **97:** 911-919

9.Hoogendoorn EH, Cools BM. Hyperthyroidism as a cause of persistent vomiting. *Neth J Med* 2004; **62:** 293-296.

10.Bassotti G**,** Pagliacci MC, Nicoletti I, Pelli MA, Morelli A. Intestinal pseudoobstruction secondary to hypothyroidism. Importance of small bowel manometry. *J Clin Gastroenterol.*1992; **14:** 56-58

.

11.Cash BD, Schoenfeld PS, Chey WD. The utility of diagnostic tests in irritable bowel syndrome patients: a systematic review. Am J Gastroenterol. 2002; 97:2812–9. [PubMed: 12425553].

12. Hamm LR, Sorrells SC, Harding JP, Northcutt AR, Heath AT, Kapke GF, Hunt CM, Mangel AW. Additional investigations fail to alter the diagnosis of irritable bowel syndrome in subjects fulfilling the Rome criteria. Am J Gastroenterol. 1999 May;94(5):1279-82.

13.Hoogendoorn EH, Cools BM. Hyperthyroidism as a cause of persistent vomiting. *Neth J Med* 2004; **62:** 293-296

14.Karaus M, Wienbeck M, Grussendorf M, Erckenbrecht JF, Strohmeyer G. Intestinal motor activity in experimental hyperthyroidism in conscious dogs. *Gastroenterology* 1989; **97:** 911-919.

15.Tenore A, Fasano A, Gasparini N, Sandomenico ML, Ferrara A, Di Carlo A, Guandalini S. Thyroxine effect on intestinal Cl-/HCO3- exchange in hypo- and hyperthyroid rats. *J Endocrinol* 1996; **151:** 431-437.

16.Thomas FB, Caldwell JH, Greenberger NJ. Steatorrhea in thyrotoxicosis. Relation to hypermotility and excessive dietary fat. *Ann Intern Med* 1973; **78:** 669-675.

17. Greenspan FS, Rapaport B. Thyroid gland. In Basic and Clinical Endocrinology FS Greenspan, JD Baxter (eds). Norwalk, Connecticut, Appleton and Lange, 1992: 188-246.

18.Jalal NA, Al-Samarrai AH, Al-Tikriti KA. biochemical changes in patients with hyperthyroidism. *Tikrit Journal of Pure Science Vol. 15 No.(1) 2010.*