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Review Article

# Study of the Interrelationship Between Irritable Bowel Syndrome and Hypothyroidism

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## Abstract

Irritable bowel syndrome (IBS) is becoming popular health problem day by day. Report shows that around15 to 25% of the world population suffers from IBS. There is lack of evidences where gastrointestinal manifestation is reported with thyroid dysfunctional state, yet in this regard gastrointestinal motor dysfunction, predisposes with altered intestinal motility as well as transit time, has been accepted as the leading cause of gastrointestinal symptoms of thyroid disease. Research shows that patients having hypothyroidism may also experience frequent bowel movements, diarrhea, along with malabsorption and steatorrhea. epigastric pain and fullness etc such chronic dyspeptic symptoms as well as eructation, nausea and vomiting are also frequently observed among such patients. After all it is still not clear whether thyroid disorder can be considered in the differential diagnosis of patients with IBS symptoms or not. Hence in present review the objective was to understand the interrelationship between irritable bowel syndrome and hypothyroidism. The routine thyroid function tests in the diagnostic evaluation of established IBS patients should be recommended since it has been observed that hypothyroid patients have a great risk of developing IBS in the long run. More elaborative evidence based research is required to understand the relationship clearly.

**Keywords**: Irritable bowel syndrome, gut microbiome, psychosocial status, GI motility.

## Introduction

Irritable bowel syndrome (IBS) is becoming popular health problem day by day. The IBS can be characterized through a large extent on symptoms, gastrointestinal manifestations of patients. Although there is lack of evidences considering research reports yet the thyroid disorder can be considered in the differential diagnosis of patients with IBS symptoms. Report shows that around15 to 25% of the world population suffers from IBS [1]. Abdominal discomfort or pain is the classical characteristics of IBS [1,2], again changes in bowel habit and abdominal bloating will also be present in it. According to the classification IBS can be of 4 classes. Which are IBS with diarrhea-predominant features (IBS-D), IBS with constipation-predominant features (IBS-C), IBS with normal consistency [3] stool (IBS-U) and IBS with mixed pattern of stool (IBS-M) [3]. Identification of IBS is still lacking in appropriate biological markers; hence the diagnostic definitions as well as classifications have relied to a large extent on symptoms [3-5]. Typical characteristics of symptoms include persistent or recurrent abdominal pain related to defecation and/or chronic disturbance of bowel habits [3-5]. There is lack of evidences where gastrointestinal manifestation is reported with thyroid dysfunctional state, yet in this regard Gastrointestinal motor dysfunction, predisposes with altered intestinal motility as well as transit time, has been accepted as the leading cause of gastrointestinal symptoms of thyroid disease

[6]. Research shows that patients having hypothyroidism may also experience frequent bowel movements, diarrhea, along with [6-8] malabsorption and steatorrhea. epigastric pain and fullness etc such chronic dyspeptic symptoms as well as eructation, nausea and vomiting are also frequently observed among such patients. Persistent and intractable vomiting may also be present among such patients though it is less common [9]. Furthermore decreased metabolic function is observed in patients having hypothyroidism. Again manifestation of sluggish intestinal motility, ranging from mild constipation to paralytic ileus as well as colonic pseudo-obstruction [10]. After all it is still not clear whether thyroid disorder can be considered in the differential diagnosis of patients with IBS symptoms or not [10-20]. Hence in present review the objective was to understand the interrelationship between irritable bowel syndrome and hypothyroidism.

## Data synthesis

Relevant traditional, contemporary and up-to-date literature was collected via extensive literature searches of authentic databases, including PubMed, Google Search, Google Scholar, Research Gate and cross-references using keywords: Irritable Bowel Syndrome, Diet, Hypothyroidism, Constipation, Defective gut immune function, gastric motility etc. The inclusion criteria were (i) Irritable Bowel Syndrome, (ii) Hypothyroidism, (iii) Obesity (iv) GABA (gamma-aminobutyric acid) (v) Depression. Potential studies with original data were selected and their important findings were incorporated into the methodology. The method of identification, screening and selection of literature is summarized in figure 1.

## Irritable bowel syndrome (IBS)

IBS stands for Irritable Bowel Syndrome which is one of the most commonly diagnosed gastrointestinal diseases affecting the large intestine. Some of the most commonly seen symptoms of this disease are cramping, bloating, gas, abdominal pain, diarrhea or constipation or sometimes both together [11-13]. IBS is 1.5 times more commonly seen in women as compared to men as well as mostly diagnosed in the lower socioeconomic group, before the age of 50 years. This chronic disease reduces the quality of life, work productivity and needs a long term treatment [14,15]. Cases of IBS in India are seen to be more than 1 million/year. The most common signs and symptoms of this disease include diarrhoea, constipation, gas and bloating, food intolerance, cramps, depression, etc. [16,17]. According to recent research the factors associated with IBS is mentioned in figure 2 [15].

## Hypothyroidism and IBS an overview

Hypothyroidism is that condition of the body when the thyroid gland does not produce enough thyroid hormone due to the lack/deficiency of iodine in the body. This deficiency of thyroid hormone can disrupt certain normal bodily functions like heart rate, body temperature along with all aspects of metabolism. Some of its major symptoms include fatigue, cold sensitivity, dry skin and an unexpected gain in weight. Hypothyroidism is most prevalent in women and is the second most common endocrine disorder that is diagnosed in this specific gender group. Treatment of hypothyroidism includes thyroid hormone replacement [18]. Cases in India are seen to be more than 10 million/year.

Hypothyroidism affects all parts of the GI tract, inducing certain problems to disrupt the normal functioning of the stomach in the body. Some of the dysfunctional stomach symptoms are stated in figure 3 [18].

## The relationship

There have been quite a lot of studies to prove that a malfunctioning thyroid has a direct impact in the gut. One such study states that there are numerous gastrointestinal symptoms associated with a dysfunctional thyroid (as mentioned under the topic above), which involves all the parts of the GI tract in the patient [19].

In hypothyroid patients, there is a reduction in the esophageal and gastric motility which leads to reduced appetite as well as constipation. The effect of this reduced motility is the increased bacterial growth in the small intestine. This high population of bacterial residents induces diarrhea in the patient along with the continuation of the cycle of bowel disturbance. This overgrowing bacteria can also lead to symptoms of flatulence, bloating and abdominal discomfort [19]. With regards to the above stated point, the abdominal discomfort and bloating are so severe that they can often be mistaken as symptoms of functional bowel disease in the patient. It is commonly observed that hypothyroid patients suffer from severe bloating accompanied by the regular feelings

of tiredness and coldness. These patients always complain about the feeling of fullness, food hanging in their chest and persistent bloating, even after following a careful and strict diet. All of these indicate a malfunctioning thyroid [19]. It must be surprising to know that levothyroxine, one of the thyroid medicines, itself causes bloating and discomfort in certain patients. One of the major ingredients included in this medicine is lactose which can be problematic for all lactose intolerant hypothyroid patients.

## Identification

**Figure 1:** Flowchart of the Methods used.

These patients are unable to digest the lactose and suffer from abdominal discomfort, nausea, vomiting, bowel disturbance as well as gas. All of these symptoms are very much similar to that of IBS and celiac disease [19]. There's a marked reduction in the bile flow in all hypothyroid patients. This reduced bile flow has a direct impact on the fat metabolism in the patient's body. Thus, an evident gain in weight is seen in all the patients proving that hypothyroidism has a direct impact on the fat digestion [19]. The risk of pathological development in the gastrointestinal system increases in all hypothyroid patients. This condition arises either due to disturbance in the thyroid hormone levels or can be related particularly to the thyroid disease itself [21]. All of the above mentioned symptoms are similar to IBS as well as the IBS symptoms like bloating, constipation, diarrhoea, fatigue and abdominal pain are very much similar to that of hypothyroidism [21]. It must also be noted that hypothyroidism doesn't cause IBS but it definitely worsens the symptoms of the latter. hypothyroidism slows down the gastric emptying time leading to symptoms of nausea, stomach distention and acid reflux. Hypothyroidism also reduces the stool frequency so one can expect a hypothyroid patient to suffer from constipation, a well known symptom of IBS [21].

**Figure 2:** Factors leading to Irritable Bowel Syndrome (IBS) [15,42].

## Statistics related to IBS and hypothyroidism

Now, let's look into some important statistical data related to both IBS and hypothyroidism. The rate of clinical hypothyroidism is 0.5%-1.9% in women &<1% in men [18]. The rate of subclinical hypothyroidism is 3%-13.6% in women and 0.7%-5.7% in men [18]. IBS affects 7%-21% of the general population [15]. 19%-20% of the general population in India and USA show prevalence of thyroid dysfunction in IBS [20].

**Figure 3:** Dysfunctional stomach symptoms associated with hypothyroidism [18].

### Impact of thyroid treatment on IBS

Through many clinical studies, hypothyroidism has been found in many IBS patients, wherein the former either masks its symptoms or is the causing agent of the latter. In most cases, hypothyroidism causes constipation which may get misdiagnosed as IBS since it's one of its symptoms as well. In the process of treating hypothyroidism, constipation may also get cured but it might lead to the emergence of diarrhoea. This might make it seem that the patient was overdosed with the treatment to relieve hypothyroidism and it led to diarrhoea. But, it may not be the case. The treatment dose is likely to be correct but while relieving the patient of constipation, it led to the unmasking of IBS with diarrhoea also known as IBS-D, which was suppressed by the constipation symptom of hypothyroidism [19,21].

### Hypothyroidism, IBS and food sensitivity

A hypothyroid patient shows insufficient levels of T4 and T3 thyroid hormones. T3 is the active thyroid hormone that is derived from the inactive T4 thyroid hormone, which plays an active role in maintaining the intestinal lining. The lack of this T3 thyroid hormone causes immune dysregulation along the gut lining, downregulates the release of digestive enzymes and finally gives rise to intestinal permeability. It has been observed that all these effects of low T3 hormones lead to food sensitivities. In all autoimmune thyroid cases, it has been observed that there is an underlying inflammatory mechanism which is responsible for dysregulating the conversion of inactive T4 thyroid hormone to its active component T3 thyroid hormone. Such inflammatory mechanisms are namely, chronic stress, poor dietary habits, gluten sensitivity, imbalanced microbiome in the body, any viral infection like the Epstein-Barr virus, or continued exposure to high levels of environmental toxins like glyphosate [22].

Certain clinical studies have shown that IBS patients show symptoms of food hypersensitivity, more specifically 65% IBS patients have been observed to show hypersensitive reactions to specific food items. This food hypersensitivity may be affected by the immunoglobulin E-dependent and independent mechanisms which involve the mast cells, eosinophils and other immune cells. These patients have reported worsening of gastric symptoms after food ingestion which can be further associated with the abnormal eating habits or psychological stress [23].

### Hypothyroidism, IBS and obesity

As mentioned before, hypothyroidism leads to unwanted weight gain, ultimately leading to obesity. Obesity is a medical disorder that is very much complex to treat, whereas hypothyroidism is comparatively easier to treat. The thyroid gland produces hormones that help to regulate the basal metabolism, thermogenesis, lipid and glucose metabolism, food intake and fat oxidation [24]. With respect to these functions, hypothyroidism is related to decreased metabolic rate, decreased thermogenesis, higher body mass index (BMI) and higher occurrence of obesity. When we intake extra energy, in the form of extra calories from the food we eat, it gets stored in the body as fat. Then, a significant amount of this stored fat in the body leads to obesity, which is a chronic disorder further leading to multiple health issues [24].

However, it's not always necessary that an untreated hypothyroid patient will always develop obesity but in regards to certain studies, around 50% of hypothyroid patients experience weight gain, on an average of about 5-10 pounds gain in weight [24].

There is also a prevalence of IBS in obese patients, though still not very clear but there are a few studies to justify this statement. Certain clinical findings suggest that delayed colonic transit can cause constipation symptoms in IBS patients and there is an inverse correlation between BMI and colonic transit time in IBS patients, while segmental colonic motility disturbances can lead to the rise of diarrheal symptoms in obese patients with IBS. As stated earlier, 67% of IBS patients suffer from food hypersensitivity, which supports the possibility of ingested food being an underlying factor that raises both IBS and obesity symptoms. Some recent studies have observed IBS patients to consume more canned food, processed meat, cakes and ice cream which has potential to support the risk of obesity, along with vegetables, fruits and grains. Hence, it can be said that diet acts as a bridge to link both IBS and obesity [25].

### Hypothyroidism, IBS and GABA (gamma-aminobutyric acid)

Thyroid hormones (THs) play an important role in the development of brain and normal brain functions in all vertebrates. According to studies, hypothyroidism tends to decrease enzyme activities and GABA levels in a developing brain while in the case of

an adult brain, both of these levels increase. Again, *in vitro* studies of the adult brain have proved that the thyroid hormones enhance the GABA release while inhibiting the GABA reuptake through rapid extranuclear actions. Hence, this proves that the presence of thyroid hormones in the synapse has the ability to prolong the action of GABA after its release. The thyroid gland exhibits GABA transport mechanism as well as the enzyme activities for GABA synthesis and degradation. Also, the thyroid hormone has an extranuclear effect to inhibit the GABA stimulated chloride ion currents by a non-competitive mechanism, *in vitro* [26].

Clinical experimental studies have also observed alterations in GABA-B receptor levels in IBS patients along with a higher level of GABA-A receptor α3. These levels were mostly observed under conditions of stress and can be said that stress plays a key role in the alteration of GABA levels in such patients. Furthermore, anxiety disorders are also termed as comorbid symptoms in IBS patients. In this context, GABA levels in the prefrontal cortex have been observed to increase in IBS patients who suffer from severe anxiety symptoms, while there is no such observations in IBS patients without comorbid anxiety symptoms [27].

## Psychiatric signs and symptoms related to hypothyroidism

Over the years through clinical and research studies, many psychological symptoms have been associated with hypothyroidism, with the most common symptoms being forgetfulness, fatigue, mental slowness, inattention and emotional lability [28]. Among all these, depression is proven to be the predominant affective disorder in hypothyroid patients. These patients also suffer from certain perpetual changes with their taste, hearing and vision. Delusion and hallucination might also occur in some patients. The existence of these neuropsychiatric symptoms is related to the fact that most of the hormones of the human body are related to the central nervous system (CNS), either they are synthesised within the CNS or at a distant point as well as across the blood-brain barrier. The brain is known to have a unique sensitivity to the thyroid hormone and utilises it differently than the other organ systems of the body. High concentrations of the T3 receptors are found in the amygdala and hippocampus regions of the brain, which influences all neural activities [28].

## Hypothyroidism and serotonin

The serotonin system of the body is important in the pathogenesis of depression and it is being speculated that this serotonin system is also involved in the mood harmonising effects of the thyroid hormones, among patients who show affective disorders. Thyroid hormones are found to be more effective among patients with affective disorder, when they are administered as a collateral treatment to antidepressant and/or mood stabilisers that perturb the serotonin system [29]. Human neuroendocrine challenge studies in hypothyroid patients have shown that a reduced 5-HT (hydroxytryptamine) responsiveness is reversible through replacement therapy. When thyroid hormones were administered in animals with experimentally induced hypothyroid states, the effect observed was an increase in the 5-HT concentrations along with the desensitisation of the auto-inhibitory 5-HT1A receptors in the raphe area. This resulted in the unconstrained release of the cortical hippocampal 5-HT. The thyroid hormones also increased the cortical 5-HT2 receptor sensitivity and thereafter, it can be said that the thyroid economy had a harmonising effect on the brain serotonin system [21].

## Hypothyroidism and depression

As mentioned earlier, depression is the major affective illness for thyroid patients. It has helped to establish a strong relationship between hypothyroidism and disturbance in mood. According to studies, approximately 40% of the clinically hypothyroid patients show signs and symptoms of depression [29]. Furthermore, in a meta-analysis approximately 50% of the patients with refractory depression showed evidence of subclinical hypothyroidism [31]. Treatment-resistant depression has also been shown to respond to thyroid hormone supplementation without laboratory investigation, which shows evidence of thyroid malfunction. Subclinical hypothyroidism can also make patients suffering from major depression less responsive to anti-depressant treatment [30].

## IBS and psychobiotics

Anxiety and depression are common symptoms in patients suffering from GI disorders. The prevalence of anxiety and depression was reported to be found in 20-60% IBS patients. According to a previous Vietnamese study, anxiety and depression

was found to be in 60% of IBS patients [32]. It is possible that GI patients, who are suffering from anxiety and depression might benefit from the usage of probiotics in order to improve the gut microbiome. This is proven with respect to the link present between gut microbiome, the gut-brain axis and the psychiatric symptoms [33]. Among the many probiotics, *Bifidobacterium*, *Lactobacillus* and *Lactococcus* [34] have the ability to improve anxiety and depression symptoms. The mechanism of these psychobiotic strains can be better understood by the combination of various protective mechanisms, which includes the enhancement of the barrier of the intestinal epithelium, inhibition of the mast cell activation, stimulation of the anti-inflammatory cytokines and reduction of the lipopolysaccharide levels, that play an important role in the pathogenesis of depression and other mental illness [35,36].

### IBS and depression

IBS and mood disorders like depression are two overlapping conditions with 60% of the IBS patients showing signs of lifetime depression. The neurotransmitter serotonin is known to play an important role in linking IBS with depression. Dysfunction of the gut-brain axis along with some genetic factors like, food sensitivities, infections or allergies are said to be parts of the pathophysiology of IBS and depression [37,38]. Symptoms of IBS include a level of distress that seems very much similar to that of depression. Some IBS patients get so worried about the worsening of their diarrhoea, constipation or other symptoms, that they start avoiding schools, work or outings. They start focusing less on their social lives and lose interest in those activities that they once enjoyed [12,39]. They turn restless and irritable, which are symptoms of depression. Also, these mood disorders might influence the way these patients handle their IBS since they feel too tired or hopeless to bother about their diet to ease the digestive symptoms or they start to think that they won't be able to treat their constipation or diarrhoea. Emotional stress also makes bowel disorders worsen [41]. The rate of lifetime depression in IBS patients is found to be 60%, which makes depression the most common psychiatric disorder in IBS. Also, 27% of the depressive patients show symptoms of IBS [16,40].

## Conclusion

Neither IBS nor hypothyroidism is the causing agent of the other disease/disorder, hypothyroidism symptoms definitely worsens the conditions of IBS. Both IBS and hypothyroidism share some similar symptoms that involve the gastrointestinal (GI) tract of the suffering patient including depression, which is the most effective psychiatric disorder in both the cases as well. The routine thyroid function tests in the diagnostic evaluation of established IBS patients should be recommended since it has been observed that hypothyroid patients have a great risk of developing IBS in the long run. More elaborative evidence based research is required to understand the relationship clearly.

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## Conflict of Interest

The authors declare no conflict of interest.

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