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# Vomiting, Nausea, and Abdominal Pain: Unrecognized Symptoms of Thyrotoxicosis

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*The prevalence of symptoms in thyrotoxicosis at the time of diagnosis has received little attention in studies of this condition. Vomiting, nausea, and abdominal pain have not been included as common presenting symptoms for thyrotoxicosis in standard textbooks of medicine and endocrinology. Some reports in the medical literature, however, indicate that these abdominal symptoms may be important manifestations of this condition. A retrospective chart review was undertaken to determine the prevalence of vomiting, nausea, and abdominal pain in patients hospitalized for thyrotoxicosis at Louisiana State University Medical Center, Shreveport, from 1982 through 1986. Of 25 thyrotoxic patients who had thyrotoxicosis diagnosed during or immediately prior to admission, 44% reported vomiting, 28% reported nausea, and 20% complained of abdominal pain. One or more of these abdominal symptoms were included as a chief complaint in 36% of cases reviewed. Further study of the clinical presentation of thyrotoxicosis in the outpatient setting is needed to improve the timeliness and cost effectiveness of the clinical diagnosis of this condition.*

**T**he clinical presentation of thyrotoxicosis, like many other common conditions, continues to be of primary importance in cost-effective diagnosis.<sup>1,2</sup> Although descriptions of the signs and symptoms of thyrotoxicosis are readily available in the medical literature, these descriptions are based on very few published studies. In 1946, Williams<sup>3</sup> reported the frequencies of signs and symptoms of thyrotoxic patients in a study of the effectiveness of thiouracil. This report continues to be the most widely quoted study on the clinical manifestations of thyrotoxicosis.

A need for further study in this area was recognized when several thyrotoxic patients came to the Louisiana State University Medical Center in Shreveport with vomiting as a primary symptom. This presentation was unexpected, since vomiting was not included as a symptom of thyrotoxicosis in Williams's report. Current textbooks ei-

ther fail to include this symptom or describe it as occurring rarely or only preceding thyroid storm.<sup>4-7</sup> Several other reports in the medical literature, however, indicate that vomiting, as well as nausea and abdominal pain, are more common symptoms of thyrotoxicosis than is generally recognized.

Vomiting was a prominent symptom in a case reported by Sir William Osler in 1907,<sup>8</sup> and, in 1930, Freund and Cooksey<sup>9</sup> reported five cases of thyrotoxicosis in which vomiting was the predominant symptom. Vomiting and abdominal pain were frequent symptoms in 34 cases of masked gastrointestinal hyperthyroidism reported in 1931 by Verbrycke.<sup>10</sup> In 1973, Rönnov-Jessen and Kirkegaard<sup>11</sup> reported a series of 49 patients hospitalized for thyrotoxicosis, with nausea and vomiting present in 16% and abdominal pain in 14%. In the following year, in a prospective study of 121 hospitalized thyrotoxic patients, Gordon et al<sup>12</sup> reported nausea or vomiting in 29% and abdominal pain in 22%. Numerous case reports of vomiting and abdominal pain due to thyrotoxicosis have continued to be published.<sup>13-18</sup> Thyrotoxicosis has also been implicated as a causative factor in hyperemesis gravidarum.<sup>19-22</sup>

The purpose of this study was to determine the prevalence of vomiting, nausea, and abdominal pain as symptoms in patients hospitalized for thyrotoxicosis.

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## METHODS

A computer search identified 75 patients with a primary discharge diagnosis of thyrotoxicosis hospitalized at Louisiana State University Medical Center in Shreveport (LSUMC-S) from January 1982 through December 1986. The author reviewed admission histories and consultants' reports on all charts that met all of the following criteria:

1. Patients were nonpregnant adults.
2. Thyrotoxicosis was a new diagnosis made during the hospitalization or within 2 weeks prior to admission.
3. Charts contained at least one complete history and physical examination recorded by a family practice or internal medicine resident.
4. An endocrinology consultant report was recorded and concurred with the diagnosis of thyrotoxicosis.
5. Both thyroxine ( $T_4$ ) and free thyroxin index (FTI) were above normal range.

Charts of patients on chronic  $\beta$ -blocker therapy were excluded because symptoms are suppressed by this medication. Previously diagnosed thyroid disease was the most frequent reason charts were excluded from this study. Twenty-five charts met the inclusion criteria and were screened for symptoms of vomiting, nausea, abdominal pain, and other signs and symptoms of thyrotoxicosis previously reported. These symptoms and signs were recorded as present if they appeared in any of the admission notes or in the consultant's report.

When vomiting, nausea, or abdominal pain were reported, charts were additionally screened for concurrent illnesses or medications that might have explained these symptoms. Charts with these abdominal symptoms were also screened for duration of symptoms, fever, white blood cell count, calcium level, other diagnostic studies, use of antiemetics, follow-up visits after discharge, and evidence that the diagnosis had been missed on previous visits.

The prevalence of symptoms and signs from this chart review were compared with previous reports utilizing Pearson's chi-square, with Yates' correction when expected values were less than 5. Pearson correlations were used to compare the number of signs and the number of symptoms with age, sex, and level of thyroid function tests, as well as coexistence of symptoms and signs. Signs and symptoms in patients with thyroid storm were compared with those of patients without storm, using the *t* test.

## RESULTS

The age range for the 25 patients with thyrotoxicosis was 13 to 62 years, with a mean of 40 years of age. There was a 3:1 female to male ratio. The cause of hyperthyroidism was

TABLE 1. FREQUENCY OF SYMPTOMS IN THYROTOXICOSIS: CURRENT STUDY (LSU) COMPARED WITH STUDY BY WILLIAMS<sup>3</sup> (RHW)

Symptom	Percentage of patients		
	LSU	RHW	P Value
Weight loss	80	85	NS
Nervousness	76	99	*
Dyspnea	64	75	NS
Heat intolerance	60	89	*
Palpitation	48	89	*
Vomiting	44	—	
Eye complaints	44	54	NS
Swelling of legs	40	35	NS
Chest pain	36	—	
History of fever	36	—	
Increased sweating	32	91	*
Diarrhea	28	23	NS
Nausea	28	—	
Fatigue	24	88	*
Weakness	24	70	*
Increased appetite	24	65	*
Tachycardia	20	82	*
Abdominal pain	20	—	
Constipation	20	4	*
Anorexia	16	9	*
Swelling in neck	16	—	
Dysphagia	12	—	
Frequent bowel movements	8	33	*
Hair loss	4	—	

\*  $P < .05$   
NS  $P > .05$

Graves' disease in 24 patients and toxic nodular goiter in one patient; the latter did not complain of abdominal symptoms. Thyroid storm was included in the discharge diagnosis and the endocrinologist's assessment for four patients. Three of the four patients with thyroid storm complained of vomiting, and one patient reported abdominal pain. One patient with thyroid storm died, the only fatality.

The average number of symptoms and signs among these patients was 7.8 and 5.7, respectively. There was no significant correlation ( $P > .10$ ) between the number of symptoms or the number of signs and age, sex, level of  $T_4$ , or level of free thyroxine index. Patients who experienced thyroid storm did not have a greater mean number of symptoms or signs than did those who did not experience such a crisis.

Frequencies of all symptoms and signs screened for are listed in Tables 1 and 2, respectively, with results previously reported by Williams<sup>3</sup> included for comparison. The symptoms and signs reported in the present study were generally less frequent than those reported in Williams' study, but had a similar relative order.

Vomiting was reported in 44% of cases. Of the 24 symptoms studied, only five were more frequently reported than

**TABLE 2. FREQUENCY OF SIGNS IN THYROTOXICOSIS: CURRENT STUDY (LSU) COMPARED WITH STUDY BY WILLIAMS<sup>3</sup> (RHW)**

Sign	Percentage of patients		
	LSU	RHW	P Value
Goiter	92	100	NS
Tachycardia (> 100 beats per minute)	80	72	NS
Heart rate (80-99 beats per minute)	20	28	NS
Systolic murmur	76	—	—
Skin changes	72	97	*
Tremor	60	97	*
Brisk deep tendon reflexes	56	—	—
Wide pulse pressure†	52	—	—
Ocular signs	48	71	*
Bruit over thyroid	16	77	*
Atrial fibrillation	6	10	NS
Gynecomastia	14	10	NS
Splenomegaly	4	10	NS
Liver palms	0	8	NS
Onycholysis	0	—	—

\*  $P < .05$   
†  $\geq 70$  mm Hg  
NS  $P > .05$

vomiting. Nausea was reported in 28% of cases, and all patients with nausea also complained of vomiting. Abdominal pain was reported in 20% of cases, and patients with this symptom had a greater total number of symptoms ( $P < .01$ ) than patients without abdominal pain. No significant correlation ( $P > .37$ ) was found between the complaints of vomiting, nausea, or abdominal pain when matched with the levels of  $T_4$ , levels of FTI, or number of signs. Surprisingly, vomiting was not significantly correlated with the presence of abdominal pain ( $P = .44$ ) or the number of symptoms ( $P = .83$ ).

The frequencies of vomiting, nausea, and abdominal pain found in this study were compared with frequencies from studies by Rönnov-Jessen and Kirkegaard<sup>11</sup> and Gordon et al.<sup>12</sup> There was no significant difference in the frequency of abdominal symptoms found in this study when compared with each of the previous studies. Nausea and vomiting were not reported as independent symptoms in the two previous studies; therefore, data on these symptoms were grouped to allow valid comparisons.

At least one of the symptoms of vomiting, nausea, or abdominal pain was reported in 52% of cases reviewed and was listed as a chief complaint in 36% of cases. Of the 11 patients who reported vomiting, it was a chief complaint in five and chronic (> 2 weeks) in five patients. Vomiting was described as postprandial by four patients, and two patients stated it was made worse with solid foods. Vomiting occurred without nausea in four patients.

Abdominal pain was listed as a chief complaint in four of the five patients reporting this symptom. Abdominal pain was a chronic problem in three patients and acute in two patients. Pain was located in the midepigastric area in three cases and on the left side in two cases. Abdominal pain was not related to meals by four of the patients and was described as "sharp," "cramping," or "intermittent."

No concurrent illness or medication was identified to explain these abdominal symptoms in any case. White blood cell counts for each patient were within the normal range. Serum calcium was elevated in only one patient (3.24 mmol/L, 13 mg/dL) and was thought to be secondary to hyperthyroidism. Fever was present in three patients, all of whom had thyroid storm. Further studies of the gastrointestinal tract (upper gastrointestinal x-ray examination, ultrasound, and endoscopy) were performed in three patients, and all were normal. Antiemetics were used at the time of admission in only three patients, and no patients required antiemetics during hospitalization.

A review of the records from follow-up visits indicated that these abdominal symptoms resolved following treatment of hyperthyroidism. Follow-up records were available for all patients with vomiting, nausea, and abdominal pain for at least 1 month after discharge, and most patients had follow-up visits recorded for 3 to 6 months. No patient continued to complain of abdominal symptoms on these follow-up visits.

Missed diagnosis occurred on prior clinic visits in five cases. In each of these cases, abdominal symptoms were the chief complaint. The diagnosis was missed in four of five patients who complained of abdominal pain. The duration of missed diagnosis was lengthy in four patients (3 to 8 months). One patient underwent a negative exploratory laparotomy for abdominal pain 19 days before the diagnosis of hyperthyroidism. Patients with missed diagnosis had as many other symptoms and signs indicating thyrotoxicosis as did patients without missed diagnosis.

## DISCUSSION

This study indicates that vomiting, nausea, and abdominal pain are relatively common presenting symptoms in patients hospitalized with thyrotoxicosis. The frequency of vomiting found in this study surpassed that of several symptoms considered more classic of thyrotoxicosis. The sample size in this study was small because strict inclusion criteria were used to identify new cases, and this limitation weakens the ability to generalize from these data. Although the retrospective study design might give rise to a question concerning the completeness of methods employed in obtaining and recording data from patients, the evaluations performed by admitting physicians in this

study could be expected to be similar to those by other primary care physicians on patients in whom a diagnosis is still uncertain.

The frequencies of signs and symptoms, other than abdominal symptoms, are consistently lower than those reported by Williams.<sup>3</sup> This difference may be due to differences in study design. Williams reported signs and symptoms of patients with known thyrotoxicosis who were being treated with thiouracil. His study was not limited to new cases and was not intended to focus on presenting clinical manifestations. Williams's report does not specify whether his design was prospective or retrospective. If the lower frequencies in the present study are due to lack of thoroughness of the evaluating physicians, then the frequencies of abdominal symptoms being studied would be expected to be at least as high in a more controlled, prospective study.

The frequencies found for these abdominal symptoms were consistent with previous findings by Rönnov-Jessen and Kirkegaard<sup>11</sup> and Gordon et al.<sup>12</sup> In the study by Rönnov-Jessen and Kirkegaard, vomiting was reported as "nausea and vomiting," and the prevalence (16%) was apparently limited to those patients who complained of both symptoms. One might speculate that the prevalence of vomiting in the Rönnov-Jessen and Kirkegaard study would have been higher had this symptom been reported independently. Their study also included many patients with known thyroid disease who would have been excluded from the present study. They reported 16 "atypical" cases not known to have thyroid disease prior to admission, and 38% of these cases had nausea and vomiting.

This study was limited to hospitalized patients; it is not known whether nausea, vomiting, and abdominal pain occur as commonly in outpatients. It may be that thyrotoxic patients who have more severe illness or in whom the diagnosis is unclear are the ones most likely to be hospitalized. These factors may preselect a population with a higher prevalence of abdominal symptoms. Further studies in the outpatient setting are needed to address this issue.

There was evidence of missed diagnosis in five cases in which abdominal pain or vomiting was a chief complaint, despite these patients having other symptoms and signs of thyrotoxicosis. One may speculate that these abdominal symptoms distracted physicians from considering thyrotoxicosis and led to the missed diagnosis.

The mechanisms causing vomiting and abdominal pain in thyrotoxicosis are yet to be determined. Hypercalcemia has been shown to occur in some patients with hyperthyroidism<sup>23</sup> and could be implicated as a possible cause of these symptoms. However, Gordon and colleagues<sup>12</sup> found no such correlation between calcium levels and presence of vomiting or abdominal pain. In the present study, only one of 11 patients with vomiting had hypercalcemia.

Vomiting was described in a pattern consistent with gas-

tric outlet obstruction or stasis; ie, postprandial and often without nausea. Possible mechanisms for this symptom could be altered gastric motility or failure of the pyloric sphincter to function properly. Hyperthyroidism may cause a hyperperistalsis resulting in a relative outlet dysfunction. Decreased gastric motility could also cause these symptoms and has been demonstrated in one thyrotoxic patient.<sup>16</sup> In the present study, only one patient with vomiting had an upper gastrointestinal examination, and no abnormality of gastric motility or of the pyloric sphincter was identified. Another mechanism causing vomiting could be toxic substances triggering the emesis center, as suggested by Rosenthal et al.<sup>15</sup> This cause appears unlikely because occurrence of vomiting would be expected to be at times unrelated to meals, and nausea should be a more prominent symptom.

Further study of the presenting clinical manifestations of thyrotoxicosis is needed. The three studies cited for comparison in this report were undertaken for purposes other than identifying the presenting manifestations of thyrotoxicosis. A thorough literature search has failed to identify any study during the past 80 years undertaken for this specific purpose.

Because study in this area has been lacking, important symptoms of thyrotoxicosis, such as vomiting, nausea, and abdominal pain, have gone largely unrecognized. As a result, the correct diagnosis has been delayed in some patients, leading to unnecessary morbidity, suffering, and perhaps, preventable death. The need for study in this area was pointed out by Verbrycke<sup>10</sup> in his 1931 report on gastrointestinal hyperthyroidism: "When it is considered that these 34 cases were recognized in a period of three years, after attention was focused on the condition largely by having a case in my own family, it is a cause of intense chagrin to realize how many diagnoses have been missed in the last twenty years." To improve clinical diagnosis and the cost-effective use of thyroid function tests, a well-designed, prospective study of the presenting manifestations of thyrotoxicosis in an outpatient setting is needed.

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