

## Prevalence of Positive Glucose-Hydrogen Breath Test in Healthy Thai and IBS Patients

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### ABSTRACT

**Background:** Irritable bowel syndrome (IBS) is a common GI problem diagnosed by symptom-based criteria that is partly similar to those experienced by subjects with small bowel bacterial overgrowth (SIBO). Whether SIBO is associated with IBS is unclear.

**Objectives:** The aim of this study is to determine the prevalence of positive glucose hydrogen breath test, an acceptable non-invasive test for SIBO in IBS and healthy Thai patients.

**Patients and Methods:** A total of 34 diarrhea-predominant IBS patients, diagnosed by gastroenterologists at Siriraj Hospital using Rome II criteria and 34 healthy controls underwent glucose-hydrogen breath test. Breath hydrogen was analyzed at baseline and every 30 minutes for 2 hours after drinking 50 gram glucose.

**Results:** Mean baseline fasting glucose hydrogen breath test in IBS patients is  $5.53 \pm 6.56$  ppm. compared to  $4.50 \pm 3.41$  ppm. in healthy controls ( $P = NS$ ). Glucose hydrogen breath test was considered positive in 3/34 (8.8%) of IBS patients but negative in all healthy controls ( $P = NS$ ).

**Conclusions:** Prevalence of positive glucose hydrogen breath test in diarrhea-predominant IBS patients is not statistically significant compared to healthy controls. This pilot study does not show higher prevalence of SIBO, i.e. positive glucose hydrogen breath test in IBS patients.

**Key words :** Prevalence, glucose-hydrogen breath test, IBS

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## BACKGROUND

Irritable bowel syndrome (IBS) is a common chronic gastroenterological condition characterized by abdominal pain, bloating, disturb defecation that can not explain by structural or biochemical abnormalities. Altered motility, abnormal visceral sensation and psychosocial factors may interplay to cause symptoms

The prevalence of IBS is estimated to be 14-24% in women and 5-19% in men in the United States, IBS is responsible for 2.4-3.5 millions physician visit per year, so it bear a significant economic impact.

Various diagnostic criteria were used to diagnose IBS eg. Manning Criteria, Rome I Criteria and more recently; Rome II Criteria, All criteria are base on symptoms. In Clinical practice, the first step is taking history of patients to search for alarm symptoms or possibility of organic diseases to investigate patient extensively and patient who had no any suspicions, fit in criteria to diagnose IBS for effective use of medical resources, however the symptoms of IBS is partly similar to those experienced by subjects with small bowel bacterial over growth (SIBO). Study of Pimentel *et al.* Using lactulose hydrogen breath test concluded that 78% of IBS patients have evidence of SIBO and that 48% of subject whose SIBO was eradicated no longer met the Rome criteria for IBS. Mishkin *et al.*'s data not support the high prevalence of SIBO in functional dyspepsia/IBS patients, positive glucose hydrogen breath test is 13%. However; the gold standard to diagnose SIBO is jejunal fluid culture, the fluid is obtained by intubate the jejunum, then a closed tube system was use to collect jejunal fluid under sterilize technique. Jejunal fluid culture  $>10^5$  CFU/ml is abnormal. This is highly specific (100%) but insensitive and too impractical. Hydrogen breath test is an acceptable important non invasive tool to detect SIBO. Whether SIBO is partly in IBS patients diagnosed by Rome II criteria is not clear, so the aim of this study is to determine the prevalence of SIBO by positive glucose hydrogen breath test in IBS patients and healthy subject that is no data available in Thailand.

## PATIENTS AND METHODS

Patients who come to Siriraj Hospital diagnosed diarrhea - predominant IBS by gastroenterologists using Rome II criteria was reevaluate history, physical examination and Investigation; CBC, Stool examina-

tion for 3 times, and one of large bowel investigation (Barium enema, sigmoidoscopy or colonoscopy)

## Rome II Criteria for IBS defined as

Diarrhea symptom at least 12 weeks which need not be consecutive in the preceding 12 months of abdominal discomfort or pain that has two or three of these features

Relieved with defecation and/or

Onset associated with a change in frequency of stool and/or

Onset associated with a change in form of stool.

**Diarrhea predominant subtype IBS** are non of character of constipation(one or more of this feature)more than 3 bowel movement a day, loose or watery stools, urgency (having to rush to have a bowel movement)

Patients who suspected to have organic disease, pregnancy, drug abuse, taking medication induce - diarrhea; laxative, colchicin, Diuretic, antacid, medication suspension in sorbital were exclude. Control subjects are healthy volunteers who don't have diarrhea symptoms and don't take antibiotics for 2 weeks before the test. All of subjects received instructions and training for breathing technique. The technician and interpretator are blinded. All of patients and control group underwent glucose hydrogen breath test under instruction.

## Glucose Hydrogen Breath Test

Breath samples were obtained after an overnight fast, and all patients were asked to avoid eating bread, pasta, and fibers the previous evening because these foods may cause prolong excretion of Hydrogen, no cigarette smoking and physical exercise for 2 hour before and during the test. A mouth wash was performed before testing with 40 ml of Siriraj mouth wash (Chlorhexidine Solution) to eliminate the possibility of an early hydrogen peak due to interaction of glucose with oral bacteria

## Performed Test

Subjects drink 50 gram of glucose in water then end-expiratory hydrogen is measured by gas chromatography (hydrogen analysis Quintron) at baseline and 30 min interval after the test meal, Breath hydrogen 12 ppm. increase from baseline or fasting breath hydrogen more than 20 ppm, is interpreted positive test.

Table 1 Demographic Data

Characteristics	IBS Patients	Healthy Control
Age (Mean $\pm$ SD)	46.56 $\pm$ 14.48	31.97 $\pm$ 7.78
Sex (male: female)	12 : 22	12 : 22
Underlying disease		
Previous abdominal Surgery	4 (11.8%)	5 (14.7%)
Hyperthyroid	4 (11.8%)	-
Dyspepsia	8 (23.5%)	-
Diabetes	-	-
Dyspepsia + abdominal surgery	9 (26.5%)	-
Duration from diagnosis (median time/month)	24	
Stool frequency/day	3	

Table 2 Amount of Hydrogen production (PPM) collected at baseline and after 50 gram. glucose

Time (min.)	IBS	Control	p value
0	5.53 $\pm$ 6.56	4.50 $\pm$ 3.41	0.42
30	7.88 $\pm$ 9.25	4.65 $\pm$ 3.34	0.059
60	5.56 $\pm$ 4.73	3.59 $\pm$ 2.19	0.031
90	5.24 $\pm$ 4.51	3.26 $\pm$ 2.28	0.026
120	4.56 $\pm$ 4.22	3.09 $\pm$ 2.4	0.075
Interprets positive	3/34 (8.8 %)	None	0.239

### Statistical Analysis

Data were expressed as mean values + SD

Dichotomous variables were compared by Fisher's exact

### RESULTS

A total of 34 diarrhea - predominant IBS patients and 34 healthy control were enrolled. Subject are equal male: female (12:22), mean ages of IBS patients were 46.56 + 14.48 vs 31.97 + 7.71 healthy control. Underlying diseases in IBS, previous abdominal surgery are all only uterine tubal ligation, euthyroid stage in previous hyperthyroid. Median time of onset to diagnosis is more than 24 months and majority of diarrhea episode is 3 times/day (Table 1)

Table 2 show all mean amount of hydrogen production in IBS patients is higher than healthy control, with statistically significant difference at 60 and 90 minutes after patients drank glucose. Positive glucose

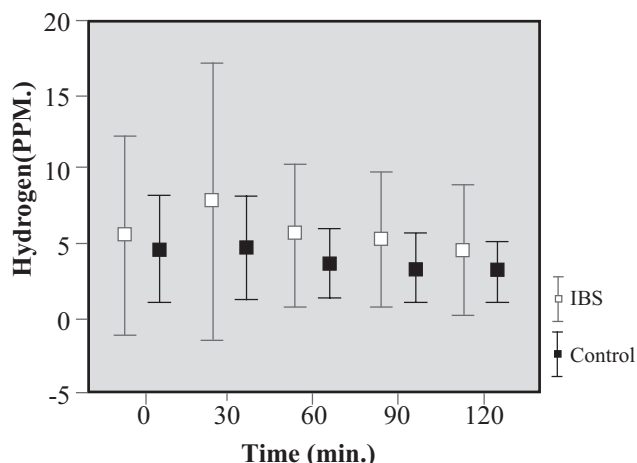
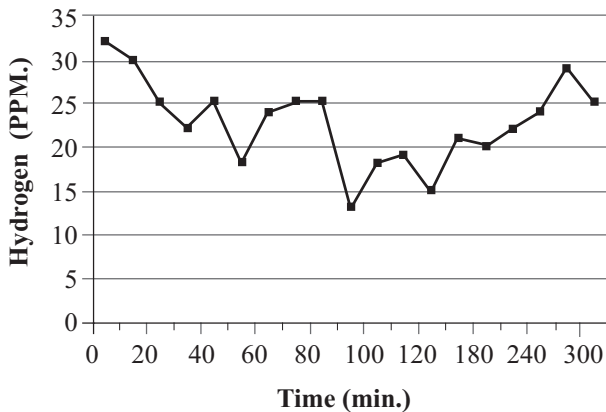


Figure 1 Show mean and rang of hydrogen production in IBS compare to healthy control at collection time

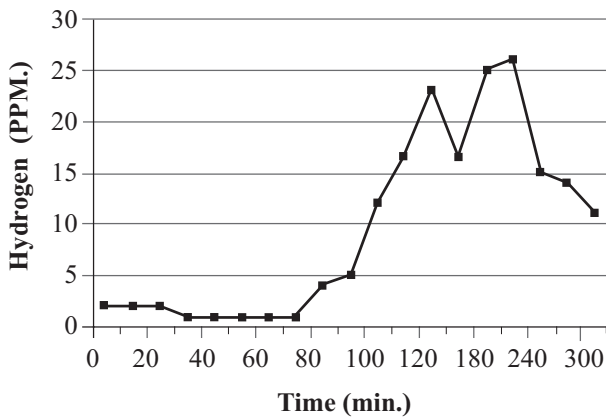
breath test in IBS is 8.8%, no one in healthy control had positive test

### DISCUSSION

Result of this study, prevalence of positive glucose hydrogen breath test in IBS is low (8.8%), don't support the high prevalence of Pimentel *et al's* study and Mishkin's study. The difference from those previous study is substrate used in breath test and study population. We preferred glucose instead of lactulose breath test in Pimentel *et al's* study because 100 % of glucose ingested is absorbed before reaching the colon even in patients with previous gastric surgery, who have faster



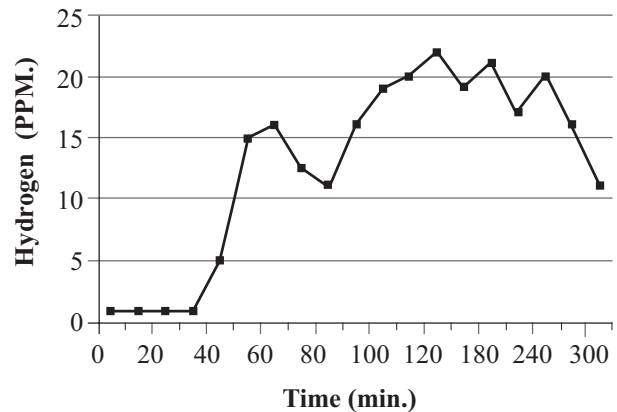
**Figure 2** Abnormal glucose-hydrogen breath test in bacterial overgrowth demonstrating high fasting breath hydrogen



**Figure 3** Normal lactulose-hydrogen breath test.

than normal transit time and any peak of hydrogen rise is positive (Figure 2) whereas lactulose; non absorbable substrate is fermented by colonic bacteria when reach the colon; in normal subject there is rising of hydrogen at 2-3 hours (colonic peak) after drinking lactulose (Figure 3), but in SIBO patients the hydrogen peak occurs within 1 hour and less prominent. So the interpretation may be complicate and can be false positive.

Glucose breath test is more sensitive and specific than lactulose breath test. In view of study populations, the patients are IBS patients diagnosed by gastroenterologists in tertiary care center (Siriraj Hospital), organic causes had been excluded by various investigations, some are investigated more than what included in the study and they had symptoms for a long times, median times to diagnosis are more than 24 months.



**Figure 4** Graph show pattern of positive lactulose hydrogen breath test

So may be the population of this study are true IBS patients, that is pretest probability for positive test is low although we selected IBS-diarrhea predominant subtype or Thai IBS patients are different in etiologies. Mechanism cause overgrowth of bacteria in small bowel is change in acidity and stasis of bowel; that is anatomy change or motility disorder; condition predispose to bacterial overgrowth such as Diabetes Mellitus, scleroderma, prolong use of acid suppression therapy but bacterial overgrowth can occur in patients who do not appear to have any predisposing condition or may have no obvious condition detected eg. motility disorder, small bowel diverticulosis. How can we find these groups that may miss diagnose as IBS by their diarrhea and bloating symptoms? Since no available simple non invasive test in detection SIBO, glucose hydrogen breath test may benefit in patients who have more predisposing condition, for no obvious predisposing condition groups, need further study to explore; perhaps higher dose of glucose (some studies use 75 gram of glucose) and more patients required. Nevertheless; this study showed statistically difference of hydrogen production in IBS patients compare to control at 60, 90 minutes after drinking 50 gram glucose but the levels don't reach criteria of positive glucose breath test.

## CONCLUSIONS

There is no association between IBS and SIBO by means of positive glucose hydrogen breath test but hydrogen production in IBS is statistically significant higher than healthy control. Mean fasting hydrogen in healthy Thai patients is  $4.50 + 3.41$ ppm.

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