



Cortisol levels in hair are altered in irritable bowel syndrome - A case control study in primary care



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ABSTRACT

Objective: Stress is an important component in the pathophysiology of irritable bowel syndrome (IBS). Long term Hypothalamus Pituitary Adrenal (HPA)-axis activity can be studied by measuring hair cortisol concentrations (HCC). Some previous studies have indicated a dysregulated HPA-axis in IBS patients, but cortisol levels in hair have not yet been studied. We investigated whether HCC and self-reported stress differentiate IBS patients from controls.

Methods: In a cross-sectional study within 10 Swedish Primary Health Care Centers we compared patients in working age with active IBS to patients without GI complaints. The participants donated hair samples and completed questionnaires including a scale of self-reported perceived stress (PSS). 169 Rome III-fulfilling IBS patients and 316 non-IBS patients were available for final analyses.

Results: IBS patients had significantly lower HCC, median = 16.3 pg/mg, IQR = 26.9 pg/mg, compared to non-IBS patients, median = 22.8 pg/mg, IQR = 29.1 pg/mg. There was also a difference in the distribution of HCC quintiles between the two groups, with 30.2% IBS patients and 14.2% of non-IBS patients in the lowest quintile of HCC. PSS was higher among IBS patients with a mean (SD) total score of 25.3 (8.0) compared to controls 21.4, (7.5). Quintiles of HCC and PSS stayed significantly but very weakly related to IBS ($B = -0.332$, Std error = 0.146, $p < 0.005$) in multivariable analyses.

Conclusion: This study suggests a possible suppression of the HPA-axis activity in a considerable portion of IBS patients.

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1. Introduction

Irritable bowel syndrome (IBS) is a symptom-based diagnosis and affects 10–25% of the general population. It has a female predominance and the majority is diagnosed in primary care [1,2]. Quality of life among IBS patients is impaired with the illness seriously affecting everyday working and social life in addition to an increased use of health care resources [3].

Stress plays a major role in the complex pathophysiology of IBS [4–6]. Early adverse life events are associated with a vulnerability to develop IBS [7]. Later on in life stress plays crucial parts in the first onset of IBS and also in the severity of gastrointestinal (GI) symptoms [8].

The individual's response to physical and psychological stress includes activation of the hypothalamic pituitary adrenal (HPA)-axis and the autonomic nervous system [9]. Corticotrophin releasing factor involved in the HPA-axis, and also expressed in the gut, modulates inflammation, visceral hypersensitivity, gut permeability and motility [10–11]. The reverse is also true and the gut influences processes in the brain [12]. This reciprocal relationship has also been suggested regarding everyday perceived stress and gastrointestinal (GI) symptoms [13].

Hypocortisolism is thought to be an important but not yet completely understood maladaptive consequence of chronic stress exposure and HPA-axis dysfunction resulting in a vulnerability to develop stress-related bodily disorders [14–15]. Exposure to chronic stress initially activates the HPA axis producing elevated secretion of cortisol but over time the activity subsides and cortisol secretion falls below normal levels [15].

A dysregulated HPA-axis in IBS-patients has previously been suggested [16]. A recent study showed lower morning cortisol levels as

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well as a reduced total release of cortisol in the morning in females with IBS compared to controls [17]. In a meta-analysis from 2011 there was no statistically significant difference in baseline levels of cortisol in IBS patients compared to controls [18]. However baseline levels of cortisol in studies are often measured just before sigmoidoscopy or rectal extensions, which may elicit acute anticipatory responses with a hyperactive HPA axis [19]. In previous studies of IBS, cortisol was measured in blood, saliva or urine. These are acute, point-in-time measures that therefore can only relate to a short preceding time interval of stress exposure [20]. However those point-in-time measures have been used to study changes in the normal diurnal rhythm and response to psychological and physiological stress [16–17]. Recently a method of measuring cumulative concentration of cortisol for longer periods has been developed through the measurement of hair cortisol concentrations (HCC) [20–21]. Cortisol is retained in the hair strands [20] that grows at an approximate rate of 1 cm per month [22]. Through extracting cortisol an index of cumulative exposure over an extended period is provided. The method has been demonstrated to be valid and reliable [23].

To date, cortisol in hair levels as a measure of HPA axis activity averaged over a period of time has not been studied in IBS. Since stress and other psychological factors, which have been shown to be relevant to IBS, are dispositional or trait characteristics, it is expected that HCC will be a relevant marker of physiologic stress response and add further information on the previously suggested dysregulated HPA-axis in IBS. We hypothesized that hair cortisol levels in IBS patients would be lower than those found in non-IBS controls and that IBS patients would demonstrate higher levels of self-reported stress.

2. Material and methods

The study adopted a case-control design in a defined region in south-east Sweden (The County Council of Östergötland). Ten Primary Health Care centers (PHCs), in the three major cities of the region, joined the study. These PHCs are responsible for primary care of a population of around 150,000 inhabitants (about 1/3 of the region). Of the three cities, one could be labeled as a white-collar city (academic) and two as blue-collar cities (industrial) [24]. The selected ten PHCs were chosen to ensure diversity concerning socioeconomic status, age of the population and number of immigrants.

2.1. Selection and inclusion process

As illustrated in Fig. 1, IBS and non-IBS control groups were identified in a two-step process. They were initially identified with ICD-10 diagnoses in the medical registers of the PHCs, then verified as meeting the ROME III criteria for IBS or not.

Patients within the normal working age range (18–65 years) with a clinical IBS diagnosis identified with ICD-10 diagnoses in the medical registers of the selected PHCs were invited by mail to participate in the study. Potential controls were identified as other patients at the selected PHCs. They were similar in terms of sex and age and had sought care for other complaints not associated with gastrointestinal (GI) symptoms and had no earlier GI diagnoses found in the patient register for the previous two years. The individuals who agreed to participate were given an appointment at the PHC, where trained staff cut a hair

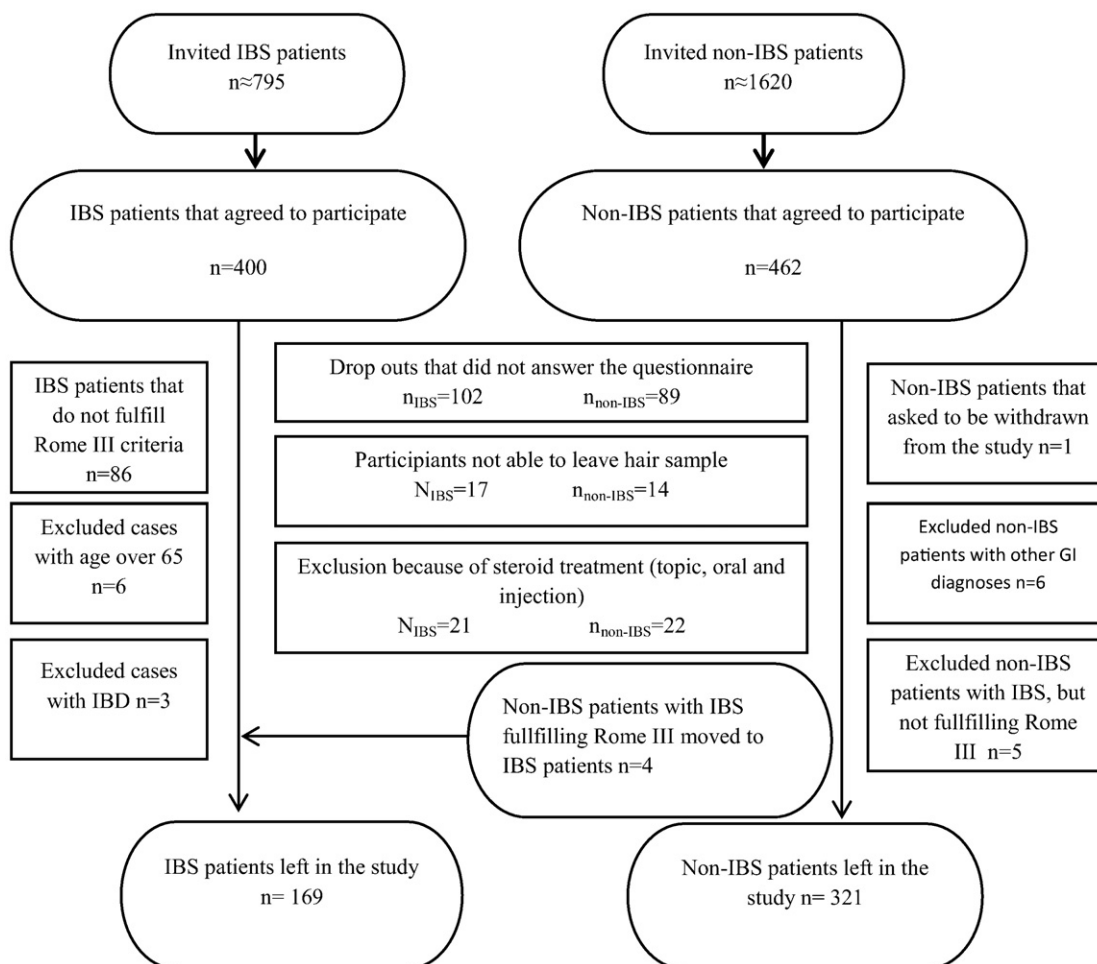


Fig. 1. Flow chart of drop-outs and exclusions.

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