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Natural History of Inflammatory Bowel Disease in Asia: A Follow-Up Population-Based Cohort Study

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Background and aim: Data on the natural history of inflammatory bowel disease (IBD) in population-based setting in Asia are scarce. It is not clear if IBD disease course differs between Asian and Western cohorts. Methods: In a population-based incident cohort from eight countries in Asia, we identified 259 IBD patients diagnosed between 2011 and 2013, including 158 ulcerative colitis (UC) and 101 Crohn's disease (CD) with a median follow-up of 15 months (range, 12-31 months). The risk of disease extent and behaviour change according to the Montreal classification, and probability of medical or surgical therapy were prospectively assessed. Results: Median age at diagnosis was 29 years (Interquartile range, IQR, 20-44) for CD, and 41 years (IQR, 30-54) for UC. At diagnosis, in CD, ileo-colonic disease (51%) and inflammatory behaviour (67%) were the most frequent phenotype. At one year, cumulative probability of behavior change from inflammatory to stricturing or penetrating disease was 18%, and cumulative rate of colectomy was 8%. In CD cumulative probabilities of receiving 5-aminosalicylic acid (5-ASA), corticosteroids, immune-suppressants and anti-tumor necrosis factor therapy were 61%, 43%, 66% and 10%, respectively, at one year. In UC, disease extent at diagnosis was evenly distributed including 31% with proctitis, 37% with left sided disease and 32% with extensive colitis. Disease extension occurred during follow-up in 19% of patients. Cumulative rate of colectomy at one year was 1%. In UC cumulative probabilities of receiving 5-ASA, corticosteroids and immune-suppressants were 91%, 28% and 13%, respectively at one year. There were two mortalities at maximal follow-up from lung carcinoma and severe sepsis. Conclusion: In this population-based follow-up study, clinical presentation and early disease course in Asian IBD patients appear comparable to that of Western patients. Progression to complicated behavior and accelerated use of immunesuppressants is common in CD. Early surgical rate for UC in Asia remains low. Understanding the natural history of IBD in our population can help optimize therapeutic interventions. Reference: SC Ng, et al. Incidence and Phenotype of Inflammatory Bowel Disease, Based on Results from the Asia-Pacific Crohn's and Colitis Epidemiologic Study. Gastroenterology 2013; 145(1):158-165.

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Pre- and Perinatal Stress and Irritable Bowel Syndrome in Young Adults - A National Register-Based Cohort Study

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Objectives: Functional gastrointestinal disorders (FGID), including irritable bowel syndrome (IBS) are common in both childhood and adulthood and are associated with impaired quality of life and substantial health care costs. The etiology of IBS is multifactorial, but poorly understood. Animal and human data suggest that adverse early life events such as pain or stress may induce long-term changes in the nociceptive circuitry but the few studies have conflicting results and studies regarding prematurity are lacking. Method: We identified all Swedish children born between 1973-1992 in the national medical birth register. We had access to all diagnostic codes for hospital based outpatient visits 2001-2009 (The Swedish patient register) and identified all individuals who were diagnosed with IBS (K58) after they had turned 18 years. Individuals with diagnoses that could have been mistaken for IBS were excluded (e.g. celiac disease, inflammatory bowel disease). We compared occurrence of pre- and perinatal stress in individuals with and without IBS using multiple logistic regression. Results: 2,080,098 children were born in Sweden between 1973-1992. After turning 18 years, 22,557 of them were diagnosed with IBS in hospital based outpatient care. Girls had an increased risk of IBS as young adults (Odds Ratio 3.24 (95% CI 3.15-3.34)). Compared to individuals in the highest education category, individuals in the median and lowest education category were at a decreased risk of IBS (0.73(0.63-0.85) and 0.81(0.70-0.95) respectively). Neither high, nor low birth weight was a risk factor for IBS in young adults. Preterm birth, postterm birth and Apgar score <7 at 5 min were all protective factors for IBS in young adults (0.80(0.75-0.85); 0.94(0.90-0.99); 0.74(0.64-0.85)). Other protective factors were neonatal distress (fetal distress before, during and/or after delivery including neonatal signs of anoxia/hypoxia), respiratory distress, transient tachypnoea, hypoglycaemia and neonatal infections (0.81(0.75-0.89); 0.58(0.45-0.75); 0.73(0.63-0.84); 0.70(0.55-0.88); 0.73(0.61-0.87)). Conclusion: In this large population-based study, variables representing pre- and perinatal stress were protective factors for IBS in young adults. Except for female sex, we found no strong pre- and perinatal risk factors for IBS in young adults.

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Depression and Anxiety Mediate the Effect of Abuse History on IBS Symptoms and Health-Related Quality of Life

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Background: Irritable bowel syndrome (IBS) is a common functional GI syndrome which manifests with abdominal pain and no organic explanation for symptoms. Histories of abuse (physical, sexual, and/or emotional) are prevalent among IBS sufferers; abuse also is known to relate to mood disorders (depression and anxiety). When present in IBS patients, and psychiatric comorbidities are associated with more severe GI symptoms and poorer health related quality of life (HRQOL). The influence of abuse on GI symptoms and HRQOL in IBS, and particularly with respect to psychiatric comorbidity is less well established. Aims: We sought to examine the effects of an abuse history on current IBS symptoms and HRQOL, examining psychiatric comorbidity as a potential mediator of the effect of abuse on these endpoints. Methods: GI outpatients were invited over a 4-year period to complete questionnaires, including: ROME III Questions to establish FGID criteria, self-reported abuse history (Life-Stress Questionnaire), mood (Beck Depression/Anxiety Inventories), and HRQOL (SF-36). Current GI symptom severity and bother were assessed using 10-cm VAS scales, and recent symptomatic days (past two weeks) were reported. Between-group differences were calculated using Chi-square and t-tests, where appropriate, and Sobel mediation analysis was performed. Results: 272 ROME-defined IBS (50.1±0.9 yrs, 81% female) and 246 non-IBS 49.9±4.4 yrs, 65% female) controls participated. IBS subjects reported more abuse compared to those without IBS: physical (18.1% vs 6.6%), sexual (15.5% vs 7.4%), and emotional (31.7% vs 16.9%) ($p<0.005$ for each). IBS subjects also had greater depression and anxiety scores ($p<0.001$) compared to controls. History of any abuse among IBS patients was associated with greater bowel symptom bother (7.3±0.2 vs. 6.7±0.2, p=0.047), severity (7.7±0.2 vs. 6.5±0.2, p=0.001), symptomatic days (9.7±0.4 vs 8.6±0.3, p=0.03), and poorer HRQOL (39.9±2.4 vs. 54.6±1.8, $p<0.001$). An additive effect of abuse was observed, such that greater IBS symptom severity (F=5.4, p=0.001) and poorer HRQOL (F=8.7, $p<0.001$) was noted with the experience of multiple forms of abuse. Mediation analyses suggested that the effect of abuse history on GI symptom severity among IBS subjects was partially mediated by anxiety (Z=4.66, $p<0.0001$) and depression (Z=4.73, $p<0.0001$). Similarly, anxiety and depression partially mediate the effect of abuse on HRQOL (Z=-5.42 and Z=-5.99, respectively, $p<0.0001$ for each). Conclusions: Abuse experiences are more common among IBS suffers, and are associated with reports of greater GI symptoms and poorer HRQOL, particularly in those having experienced multiple forms of abuse. This influence of abuse on IBS symptoms and HRQOL appears to be partially mediated by the comorbid depression and anxiety commonly seen in abuse victims.

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Visceral Abdominal Obesity As a Risk Factor for Irritable Bowel Syndrome: A Case-Control Study

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Objectives: Visceral obesity is known to be associated with increased risk of various gastrointestinal diseases including gastroesophageal reflux disease, colorectal neoplasm, and diverticulosis. But the relationship between visceral abdominal obesity and irritable bowel syndrome (IBS) is not yet studied. The aim of this study was to investigate the association between visceral adipose tissue (VAT) and the risk of IBS. Material and Methods: This case-control study was conducted in sequential 336 subjects who underwent abdominal computed tomography scan for routine health checkup form January 2012 to August 2013 at a healthcare center. Questionnare about Rome III criteria at healthcheck-up was analyzed to diagnose in enrolled subjects. Adipose tissue as a risk factor for IBS was evaluated by use of abdominal CT scan. The association between IBS and abdominal obesity measured by VAT, subcutaneous adipose tissue (SAT), VAT/SAT, body mass index and waist circumference was evaluated by logistic regression analysis. Results: The prevalence of IBS was 19.9 % (67/336). In univariate analysis, VAT, VAT/SAT, waist circumference, and female sex were associated with IBS. However, body mass index and SAT is not associated with IBS. In multivariate analysis, VAT, VAT/SAT and waist circumference were also associated with IBS. Risk of IBS was significantly higher among subjects in high (≥126cm3) than low (<80cm3) tertile of (OR: 5.59, 95% CI: 1.29-35.37, P=0.023). Risk of IBS was significantly higher in subjects with high (≥0.8) tertile than in that with low (<0.5) tertile of VAT/SAT ratio (OR: 8.69, 95% CI: 1.88-106.11, $P<0.001$). In terms of IBS-D, the same results were observed. Conclusions: Visceral abdominal obesity was found to be an independent risk factor of IBS. Key Words: Visceral adipose tissue, Visceral obesity, Irritable bowel syndrome

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GI Bowel Symptom Comorbidity in Functional Dyspepsia

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Background: Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are treated as separate clinical entities, supported by factor analysis. However, overlap between functional GI disorders has been reported and common drug classes can be used to treat FD and IBS. Less is known whether those with FD alone respond to treatment differently than those with FD-IBS overlap. **Aims:** To determine the frequency of FD-IBS overlap among patients with FD, and to determine whether those with FD-IBS overlap respond differently to antidepressant therapy. **Methods:** This NIH-funded study (DK065713) is a prospective, randomized, double-blind, placebo-controlled 12-week treatment trial conducted at 8 sites in North America that recruited 292 subjects with FD to 3 arms: 50mg amitriptyline (AMI), 10mg escitalopram (ESC), placebo (PLA). All trial participants completed a validated Bowel Disease Questionnaire (BDQ) at baseline. All participants met Rome II criteria for FD at baseline. Responses on the BDQ were utilized to determine whether individuals met criteria for IBS by Rome II criteria. Treatment response was defined by ≥5 weeks of adequate relief (y/n) of symptoms during the 12-week treatment period. The influence of IBS on treatment response was assessed by including an interaction term (IBS by treatment group) in logistic regression models adjusting for age, gender, dysmotility type, gastric emptying, satiety, HADS anxiety score, and BMI. **Results:** Of the 292 subjects with FD, 62 (21%) also met criteria for IBS: 25 (41%) IBS-C, 20 (33%) IBS-D, 6 (10%) IBS-M, and 11 (18%) undifferentiated IBS. Self-reported bowel habits among those with FD (n=285) were: 124 (43%) normal, 59 (20%) constipation, 31 (10%) diarrhea, and 71 (24%) mixed. Bristol stool form (n=286) was reported as Type 1 and 2 in 55 (19%) and Type 5, 6, 7 in 88 (31%). The association of FD alone vs. FD-IBS overlap was not significant for age (median: 43 v. 48, p=0.96), gender (27% v 18% female, p=0.13), nor delayed gastric emptying at baseline (19% v. 26% delayed, p=0.26). There was a significant association with dyspepsia subtype (66% vs. 82% dysmotility type, p=0.015). Subjects with FD-IBS overlap were not more likely to respond to antidepressant therapy than those with FD alone (test for interaction,