



# Ethnicity and the risk of development of Crohn's disease of the ileal pouch ☆,☆☆

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## Abstract

**Background:** A system-wide, multi-ethnicity study on Crohn's disease (CD) of the pouch, including Indian American (IA) patients has not been conducted.

**Aim:** To compare the frequency of subsequent development of CD of the pouch for African-American (AA), Hispanic-American (HA), IA and Caucasian patients with ulcerative (UC) undergoing ileal-pouch anal anastomosis (IPAA).

**Methods:** In this historical cohort study from our Pouch Registry, patients with restorative proctocolectomy and IPAA for IBD with identifiable, self-declared racial background (i.e. AA, HA, IA or Caucasian) were included. Univariable and multivariable analyses were performed to identify risk factors for CD of the pouch.

**Results:** The study included 235 patients: AA (N=26), HA (N=37), IA (N=22) and randomly selected Caucasian (N=150) controls. Greater number of HA and Caucasians had a history of smoking than IA (27.3% and 27.0% vs. 0;  $p=0.007$ ). Caucasians and HA were also more likely to have a family history of IBD than IA or AA (25% vs. 27% vs. 5% vs. 4%;  $p=0.016$ .) IA less frequently had extensive colitis before colectomy than Caucasians (71.4% vs. 94.0%;  $p=0.004$ ) and more frequently required anti-TNF biologics than HA (22.7% vs. 0;  $p=0.016$ ). On multivariable logistic regression analysis, AA (odds ratio [OR]=10.1, 95% confidence interval [CI]: 1.03, 1365.8,  $p=0.004$ ) and Caucasians (OR=11.1, 95% CI: 1.4, 1427.2,  $p=0.015$ ) had a higher risk of developing

**Abbreviations:** AA, African-American; CA, Caucasian American; CD, Crohn's disease; EIM, Extra-intestinal manifestations; HA, Hispanic American; HMO, Health Maintenance Organizations; IA, Indian-American; NSAID, Non-steroidal anti-inflammatory drugs; IPAA, Ileal pouch anal anastomosis; mPDAI, modified Pouch Disease Activity Index; PPO, Preferred Provider Organizations; PSC, primary sclerosing cholangitis; UC, Ulcerative colitis.

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CD of the pouch than IA. However, the event-free survival was not significantly different between the groups on Cox regression analysis, presumably due to the sample size.

**Conclusion:** Racial background may be associated with different risk for the development of CD of the pouch for patients with IBD undergoing IPAA.

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## 1. Introduction

The incidence, prevalence, and phenotype of inflammatory bowel disease (IBD) vary depending on the ethnic background.<sup>1,2</sup> Caucasians residing in the North Europe and North America have a higher incidence and prevalence of IBD than the rest of the world.<sup>1,3</sup> Recent data suggest that the incidence of both ulcerative colitis (UC) and Crohn's disease (CD) is rising in developing countries,<sup>4,5</sup> with UC being more common than CD.<sup>4</sup> In addition, studies from migrant populations suggest that the incidence and prevalence of IBD in South-Asians (Indians, Pakistanis and Bangladeshis) may in fact be higher than the indigenous Caucasian European population.<sup>6</sup> UC is more common than CD in these populations as well, a pattern similar to their native countries.<sup>7</sup> Furthermore, the phenotype of IBD differs according to the racial background. For example, Asian patients with UC have been found to less frequently have extensive colitis (21% to 45%) than other ethnicities.<sup>2</sup>

Few studies have compared the outcomes of ileal pouch–anal anastomosis (IPAA) surgery for UC between patients of different ethnic groups. A recent study from our group compared the outcome of IPAA for Hispanic non-White patients and Caucasian-Americans and showed different pre-operative characteristics of UC, but similar pouch outcomes in terms of pouchitis and pouch failure.<sup>8</sup> A separate study from our group described similar outcomes after IPAA for African-American (AA) and Caucasian patients.<sup>9</sup> A study comparing outcomes of IPAA between South Asians residing in UK and their Caucasian counterparts, however, showed a higher frequency of pouchitis in the former group.<sup>10</sup> There are no published studies on direct comparison of outcomes after IPAA with regards to the development of CD for multiple ethnicities.

It has been estimated that 2.7% to 13.0% of IPAA patients would develop CD or CD-like condition of the pouch.<sup>11–14</sup> Reported risk factors for CD of the pouch include the presence of family history of CD,<sup>15,16</sup> smoking,<sup>17</sup> longer duration of pouch,<sup>18</sup> pre-operative diagnosis of indeterminate colitis (IC),<sup>18</sup> and seropositivity for anti-*Saccharomyces cerevisiae*-IgA antibody.<sup>18</sup> A recent study showed that Ashkenazi Jewish ethnicity was associated with a greater risk for inflammatory complications of the pouch (including CD of the pouch),<sup>19</sup> suggesting a role of genetic predisposition. However, the risk for CD of the pouch in other ethnic groups has not been directly compared. We hypothesized that ethnicity is associated with a varying risk for development of CD the pouch. The aim of the study was to compare the risk for CD of pouch and other adverse outcomes of the pouch, between different ethnic groups.

## 2. Materials and methods

### 2.1. Patients

The patients for this historical cohort study were identified from our Institutional Review Board (IRB)- approved Pouchitis Registry from 2002 to 2011. Ethnicity was based on self-declared racial background. We expanded sample sizes of the HA and AA groups from our previous studies<sup>8,9</sup> by adding 14 AA patients and 1 HA patient, respectively. Caucasian controls were randomly selected from the Registry with an approximate ratio of 1:4. In addition, we included an additional group consisting of 22 Indian-American (IA) patients. Demographics, clinical characteristics, details of surgery and course of disease were obtained from the registry and by chart review.

### 2.2. Inclusion and exclusion criteria

All eligible AA, HA, IA and Caucasian IBD patients with IPAA, above age of 18 years, were included. Pouch patients with familial adenomatous polyposis, and those with an unknown or mixed racial background were excluded.

### 2.3. Study variables

Demographics, clinical characteristics of UC (duration of UC, disease extent, history of anti-TNF biologic use (before and after colectomy) and non-steroid anti-inflammatory drugs [NSAIDs], family history of IBD, extra-intestinal manifestations [EIM], and indication for colectomy), and data pertaining to pouch surgery (stage of pouch surgery and pouch configuration) were compared among the ethnic groups. Details of country of birth were recorded from the charts. When not available, patients were contacted and the necessary information was obtained for Indian patients. To assess socio-economic status we compared insurance status and type as a substitute marker. Preferred Provider Organizations (PPO) offers coverage and ability for patients to choose the physician they request. Health Maintenance Organizations (HMO) is the next best with limited ability to choose a physician. Government sponsored insurances had limited coverage and limited ability to choose physicians.

All patients had routine follow-up at the Pouchitis Clinic staffed by an IBD specialist (B.S.). Typically, we routinely followed patients with chronic pouchitis, CD of the pouch, and refractory cuffitis every 3–6 months, acute pouchitis or cuffitis every 6–12 months, and yearly for those with normal pouches.

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