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## Differential Manifestations of Inflammatory Bowel Disease Based on Race and Immigration Status

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### Abstract

**BACKGROUND AND AIMS:** The prevalence of inflammatory bowel disease (IBD) is increasing globally. In this context, identifying risk factors for severe disease is important. We examined how race/ethnicity and immigration status influence IBD manifestations, treatments, and outcomes in a diverse, tertiary-care safety-net hospital.

**METHODS:** We conducted a single-center retrospective review of all IBD inpatients and outpatients treated from 1997–2017. Using logistic regression modeling, we compared disease onset, treatment, and outcomes by race (White, Black, Hispanic, or Asian) and immigration status (US-born vs foreign-born).

**RESULTS:** A total of 577 patients were identified, of which 29.8% were White, 27.4% were Hispanic, 21.7% were Black, and 13.0% were Asian. Compared to Whites, Asians were more

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Concept and design of the study – Lea Ann Chen and Peter S. Liang. Generation, collection, and assembly of data – Ali Khalessi, Brooks R. Crowe, Gregory Rubinfeld, Jessica Baylor, Arielle Radin, Peter S. Liang, and Lea Ann Chen. Data analysis and interpretation – Ali Khalessi, Yuhe Xia, Peter S. Liang, and Lea Ann Chen. Drafting/revision of the manuscript – Ali Khalessi, Brooks R. Crowe, and Lea Ann Chen. Critical review and approval of final draft – All.

Conflicts of Interest:

The authors disclose no conflicts.

Ethical Statement:

The study was conducted in accordance with a research protocol approved by the Institutional Review Board of New York University Langone Health (NYU IRB#: S14–01393). Lea Ann Chen is the article's guarantor.

Reporting Guidelines:

STROBE.

Supplementary Materials

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likely to be male (odds ratio [OR] 2.63, 95% confidence interval [CI]: 1.45, 5.00), whereas Blacks were more likely to be diagnosed with Crohn's disease (OR 1.75, 95% CI: 1.10, 2.77) and more likely to undergo IBD-related intestinal resection (OR 2.49, 95% CI: 1.40, 4.50). Compared to US-born patients, foreign-born patients were more likely to be diagnosed with ulcerative colitis (OR 1.77, 95% CI: 1.04, 3.02). They were also less likely to be diagnosed before 16 years of age (OR 0.19, 95% CI: 0.08, 0.41), to have undergone intestinal resections (OR 0.39, 95% CI: 0.19, 0.83), to have received biologics (OR 0.43, 95% CI: 0.25, 0.76), or to have had dermatologic manifestations (OR 0.12, 95% CI: 0.03, 0.41).

**CONCLUSION:** IBD phenotype varies by race, although foreign-born patients of all races show evidence of later-onset and milder disease. These findings may aid in disease prognostication and clinical management and, furthermore, may provide insight into intrinsic and environmental influences on IBD pathogenesis.

### Keywords

Crohn's Disease; Ulcerative Colitis; Ethnicity; Health Status Disparities; Prognosis

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### Introduction

Inflammatory bowel disease (IBD) is an increasingly common gastrointestinal illness that has been estimated to affect 2.39 million individuals in the United States.<sup>1</sup> While our understanding of IBD derives mainly from White populations in North America and Europe, disease incidence and prevalence have notably increased over the past several decades in Asia, Africa, and South America.<sup>2,3</sup> Accordingly, although IBD patients in the United States are still predominantly Caucasian, a significant proportion of the patient population is now comprised of Blacks, Hispanics, and Asians.<sup>1,4</sup>

While the precise mechanism of IBD pathophysiology and the drivers of its increasing prevalence remain poorly understood, several putative environmental, behavioral, and genetic risk factors have been identified.<sup>5-8</sup> The cumulative impact of these various influences may be compositely reflected in studies of IBD based on race and immigration status. In fact, previous studies have identified associations between race and ethnicity and IBD prevalence, severity, and associated healthcare utilization, with recent studies suggesting increased health-care utilization among non-Caucasian IBD patients and less severe phenotypes among foreign-born patients.<sup>9-14</sup> Unfortunately, few genome-wide association studies to date have included individuals of non-European ancestry,<sup>15</sup> thereby limiting the understanding of racial differences in IBD behavior attributable to genetics. Furthermore, data comparing multiple racial and ethnic groups and immigration status within one study are few and may be prone to confounding from socioeconomic influences,<sup>16</sup> particularly as many non-Caucasian IBD patients in the United States have lower income and education and have decreased utilization of private health insurance,<sup>14,17</sup> all of which may impact IBD outcomes.

We therefore aimed to study IBD characteristics, treatments, and outcomes at NYC Health + Hospitals/Bellevue, the flagship hospital of New York City's public hospital network, which serves predominantly uninsured and underinsured residents, thereby minimizing

the impact of socioeconomic and geographic confounders.<sup>18,19</sup> The environment, which combines subspecialty IBD resources regardless of income, the singular racial diversity of New York City, yet the relatively similar socioeconomic status of patients, provides a highly unique opportunity to test our hypothesis that IBD manifestations and outcomes differ by race and immigration status, with milder disease among foreign-born patients.

## Materials and Methods

We identified patients with a potential IBD diagnosis [Crohn's disease (CD), ulcerative colitis (UC)] cared for at Bellevue Hospital from October 28, 1997, through October 18, 2017, using the *International Classification of Diseases, Ninth Revision and Tenth Revision* (ICD-9 and ICD-10, respectively) codes. Diagnoses were confirmed by manual chart review. Both inpatient and outpatient data were evaluated to determine IBD characteristics such as history of IBD-related surgery, IBD treatments, and the greatest extent of disease. Those with a new IBD diagnosis and those with pre-existing IBD were both included. Patients with minimal clinical data regarding their IBD history or treatment were excluded. We also collected deidentified demographic data on individuals seen at Bellevue primary care clinics in 2014 as a comparison group.

Race, ethnicity, and country of birth were determined through chart review. When discordant results were found, data documented in social work and clinical notes were considered more accurate than administrative records. As with other studies,<sup>9–11</sup> we combined race and ethnicity into a single variable consisting of 4 groups: non-Hispanic White, non-Hispanic Black, Asian, and Hispanic. Therefore, in the subsequent text describing this study, both race and ethnicity will be referred to as "race." Given the nature of our analyses, patients characterized as being multiracial were excluded, as were those from underrepresented races (eg, Native American), given their small numbers.

All clinical records available for each patient at Bellevue Hospital were used to categorize disease extent and behavior using the Montreal classification,<sup>20</sup> with classifications based on the greatest severity and extent of disease over a patient's entire disease course using combined radiographic, endoscopic, and histologic data. Other outcomes included age of diagnosis, medication exposure (biologics, immunomodulators), intestinal complications (IBD-related intestinal or colonic resection, colonic dysplasia), and extraintestinal manifestations (IBD-related arthropathy, dermatologic manifestations, and primary sclerosing cholangitis).

Given that we expected race and foreign-born status to be highly correlated, we instead constructed separate univariable logistic regression, using White and US-born patients as the reference groups. All patients born outside of the continental United States and Hawaii were considered foreign-born, including patients from the US territory of Puerto Rico. This allowed us to examine how race and foreign-born status affected the outcome variables of interest separately. To assess for the potential confounder of race in analyses of US vs foreign-born subjects, we further evaluated differences in IBD characteristics among foreign-born patients in each of the 4 racial groups. To assess for potential confounding by length of follow-up, we used one-way ANOVA followed by Tukey's post-hoc analysis

to assess for differences in the number of years between diagnosis and the last data collection time-point based on race and foreign-born status. For all analyses, the threshold for statistical significance was defined as  $P < .05$  and  $|\pm 2.0|$  for Tukey's post-hoc values, when relevant.

### Ethical Considerations

The study was conducted in accordance with a research protocol approved by the Institutional Review Board of New York University Langone Health.

## Results

### Race and Immigration Status of Study Population

We identified 1685 potential subjects by ICD-9 and ICD-10 codes (Figure A1). Following the exclusion of 1108 patients without a confirmed IBD diagnosis or with insufficient clinical data on IBD history or treatment, we were left with a total of 577 subjects, comprised of 29.8% Whites, 27.4% Hispanics, 21.7% Blacks, 13.0% Asians, 3.8% uncommon or other (eg, multiple) races, and 4.3% unknown. The 47 individuals of uncommon, other, and unknown races were excluded, as were 5 subjects who could not be categorized into either UC or CD, thus leaving a total of 525 subjects for statistical analyses (Figure A1, Table 1). From this group, 260 patients had a confirmed country of birth, with 69.6% being foreign-born. These patients represented countries from all continents except Antarctica (Tables 2 and 3), with the majority of patients being from South America, Africa, and Asia. The number of years between IBD diagnosis and last documented follow-up in the electronic medical records was evaluated to assess for potential bias based on length of follow-up and was found not to be statistically different between races (White 10.4, Hispanic 7.9, Black 9.5, Asian 7.6,  $P = .05$ ) nor by foreign vs US-born status (foreign-born 7.7, US-born 8.3,  $P = .28$ ).

### IBD Characteristics by Race, Relative to White Subjects

Compared to White patients, Asian patients were more likely to be male (odds ratio [OR] 2.63, 95% confidence interval [CI]: 1.45, 5.00) and more likely to be foreign-born (OR 10.13, 95% CI: 3.34, 44.12), while Black patients were more likely to have CD (OR 1.75, 95% CI: 1.10, 2.77) and more likely to have IBD-related intestinal resections (OR 2.49, 95% CI: 1.40, 4.50). Furthermore, Black patients were more likely than White patients to have ever had an IBD-related colonic resection (OR 2.52, 95% CI: 1.24, 5.26).

### UC and CD Characteristics by Race, Relative to White Subjects

Among UC patients, Asians were more likely than White patients to have isolated proctitis (OR 10.34, 95% CI: 1.58, 203.08). Among CD patients, Hispanics were more likely than Whites to be diagnosed after 40 years of age (OR 1.44, 95% CI: 1.13, 6.53). There was no significant difference in perianal disease based on race.

### IBD Characteristics Based on Immigration Status

Patients who were born outside of the United States were more likely to have UC than CD (OR 1.77, 95% CI: 1.04, 3.02), and less likely to have a pediatric onset to their IBD diagnosis (OR 0.19, 95% CI: 0.08, 0.41). Furthermore, foreign-born subjects were less likely to have ever used biologics (OR 0.43, 95% CI: 0.25, 0.76), to be diagnosed with any dermatologic manifestations of IBD (OR 0.12, 95% CI: 0.03, 0.41), or to have any IBD-related intestinal resection (OR 0.39, 95% CI: 0.19, 0.83), or specifically an IBD-related colonic resection (OR 0.22, 95% CI: 0.09, 0.53). Among CD patients, foreign-born patients were less likely to have been diagnosed before 16 years of age [Montreal A1] (OR 0.12, 95% CI: 0.04, 0.34) and more likely to be diagnosed after 40 years of age [Montreal A3] (OR 9.92, 95% CI: 2.72, 64.02).

### IBD Characteristics of Foreign-Born Patients Stratified by Race

We confirmed an association between race and foreign-born status ( $P < .001$ ), with 91.3% of Asians in the study populations being born outside of the United States. However, to determine if there were other racial confounders in comparisons of US and foreign-born subjects, we further evaluated statistically significant variables by examining racial distributions in only foreign-born subjects. We found that no single race accounted for the decreased use of biologics, intestinal resections, or dermatologic manifestations among foreign-born patients. Foreign-born White, Hispanic, and Asian patients were less likely to have pediatric onset of IBD compared to their native-born counterparts. In contrast, foreign-born Black patients were as likely to have pediatric IBD as native-born Black patients. In addition, foreign-born Black patients were more likely to have UC than CD (67% vs 30%), although this finding did not reach statistical significance ( $P = .053$ ).

### IBD Population in Comparison to the Primary Care Population

To understand the demographics of our IBD population in reference to the general population of our study site, we evaluated 33,247 unique individuals who presented for evaluation in the primary care clinics of Bellevue Hospital in 2014. Again, those with races that were uncommon (0.6%), reported as “other” (11.0%), or unknown (15.5%) were excluded, leaving 24,236 primary care patients (Figure A2). In comparison to the entire primary care population, our IBD population had a higher proportion of males (62.6% vs 43.5%,  $P < .001$ ), as well as a higher proportion of White (29.8% vs 8.9%), and Black patients (21.7% vs 13.2%), as well as fewer Hispanic (27.4% vs 34.8%) and Asian patients (13.0% vs 16.0%) (all  $P < .001$ ).

## Discussion

The increase in the incidence of IBD, both in the United States and globally, presents an important opportunity to study IBD behavior by race and immigration status to better understand intrinsic (ie, host-based) and environmental influences of IBD risk and phenotype. We found that certain aspects of IBD behavior were common in specific races and that, regardless of race, patients born outside of the United States were more likely to have UC as well as milder disease.

We also found a decreased risk of IBD among Asian females, which mirrors emerging reports from populations across Asia,<sup>21–23</sup> as well as studies of Asian populations in the United States and Canada.<sup>24,25</sup> We therefore suspect that this relative protection may be inherent to Asian females and hypothesize that it may be driven by genetic factors.

We also hypothesize that environmental influences drive IBD behavior, as our foreign-born patients were more likely to have UC as opposed to CD for each race analyzed. While other studies have similarly identified a predominance of UC over CD in countries with emerging IBD,<sup>3,7,13,21,22,26–29</sup> it was unclear if this finding was an artifact given the higher level of diagnostic technologies needed to identify Crohn's and, in particular, isolated small bowel disease. Since access to diagnostic resources is largely uniform in our medical center, regardless of insurance status or ability to pay, our results suggest the predominance of UC in emerging IBD populations is a true biologic phenomenon.

Our analyses further suggest that individuals born outside of the United States develop less aggressive IBD, as measured by age of onset, treatment with biologics, dermatologic manifestations, and the need for IBD-related intestinal resections, despite having similar access to care and a similar length of follow-up compared to US-born patients. While we note the trend toward significance in terms of length of follow-up by race, there was no such trend based on foreign-born status. Previous studies assessing altered disease risk following immigration have highlighted the impact of environmental exposures on certain gastrointestinal disorders, such as colon cancer.<sup>30–33</sup> Few studies, however, have been published evaluating the impact of immigration on IBD, and results have been conflicting,<sup>34–36</sup> though this may be related to differences in duration of time since immigration. For example, a recent study by Agrawal et al demonstrated that, compared to native-born Danes, first-generation immigrants have a lower risk for IBD when immigrating from lower-risk countries. This difference in risk disappeared as the duration of residence within Denmark increased.<sup>37</sup> As our study was performed in a large single-center safety-net hospital with less than 10% of patients having access to commercial insurance, our study design minimized socioeconomic confounders and furthermore allowed comparisons across multiple races, which allows greater confidence in concluding that less aggressive IBD behavior correlates specifically with foreign-born status.<sup>18,19</sup>

We note with interest the change in IBD behavior among our Black patients. When analyzing our general IBD population, Black patients were more likely to have CD compared to UC, similar to previous studies of African American IBD patients in the United States.<sup>4,38–41</sup> However, the majority of our foreign-born Black patients had UC, matching the UC predominance found in foreign-born White, Hispanic, and Asian patients. Furthermore, the general Black IBD population had features suggesting aggressive disease, such as increased risk for surgical resections, though these findings were not true of the foreign-born Black population. While this may be partially attributed to the higher risk of surgery for those with CD compared to UC,<sup>42</sup> we believe these stark differences in IBD behavior within one race may highlight differential exposures to environmental factors, such as diet and environment, that influence risk and are altered with immigration.<sup>8,43–49</sup> These influences may potentially be mediated by the gut microbiome, which has been shown to change quickly following immigration,<sup>50</sup> and may furthermore be time-dependent,

as studies have shown that the age of exposure may influence the risk and rate of IBD development.<sup>51–56</sup> Differences in genetic background may be another potential explanation for the variation in IBD behavior among United States and foreign-born Blacks, since the admixture of genetic risk alleles prevalent in Caucasian populations is noted in African-Americans<sup>39,57,58</sup> and since the proportion of foreign-born subjects was the smallest for Black patients compared to the other racial groups we studied.

The primary strength of our study is the large and diverse patient population. This has allowed us to simultaneously assess race and immigration status within a single institution and within similar socioeconomic demographics, thus minimizing confounders such as practice variability, income, and access to care. Several limitations should be noted. First, documentation of race in medical records may be prone to inaccuracy, and retrospective chart reviews are limited by variations in data capture. Second, the relatively large proportion of Asian and Hispanic patients who were also foreign-born decreased our ability to attribute disease variations definitively to either race or immigration status. Third, a small number of foreign-born patients immigrated from developed countries with established IBD risk, which may have led to underestimating the impact of immigration. Finally, as the age of immigration was often not available for foreign-born patients, we were unable to assess differences in phenotype based on length of residence in the United States.

## Conclusion

The differences in IBD behavior identified in our study support the importance of developing a deeper understanding of the impact of race and immigration on IBD behavior, given not only the rise of disease incidence worldwide but also the increasing patient diversity within many IBD practices. In our single-center retrospective review of IBD patients at a diverse tertiary care center, we noted that IBD phenotype differed not only by race but also by immigration status. Specifically, we noted that immigrant patients presented with less severe disease and were more likely to be diagnosed with UC. Further studies to mechanistically understand the reason for differential IBD risk and presentation in certain races and among immigrant patients may provide new insights into IBD pathogenesis. This can in turn help guide disease prognostication and management in a growing and diversifying IBD patient population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Data Transparency Statement:

Additional details of analytic methods can be made available upon request, but authors do not have permission to share study data.

## Abbreviations used in this paper:

<b>CD</b>	Crohn's disease
<b>IBD</b>	inflammatory bowel disease
<b>ICD-9 and ICD-10</b>	International Classification of Diseases, Ninth Revision and Tenth Revision
<b>UC</b>	ulcerative colitis

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**Table 1.**

**Inflammatory Bowel Disease Characteristics by Race/Ethnicity**

Clinical characteristics	White	Black	Hispanic	Asian
All IBD (n = 525) <sup>c</sup>				
Ulcerative colitis	99/169 (58.6%)	56/125 (44.8%)	87/156 (55.8%)	42/75 (56.0%)
Female	74/169 (43.8%)	46/125 (36.8%)	61/156 (39.1%)	17/75 (22.7%)
Foreign-born	50/81 (61.7%)	18/38 (47.4%)	64/89 (71.9%)	49/52 (94.2%)
Age of diagnosis 16-y-old	20/155 (12.9%)	15/117 (12.8%)	15/150 (10.0%)	6/71 (8.5%)
Age of diagnosis 60-y-old	9/155 (5.8%)	5/117 (4.3%)	15/150 (10.0%)	4/71 (5.6%)
Ever used biologics	49/160 (30.6%)	35/109 (32.1%)	42/148 (28.4%)	16/70 (22.9%)
Ever used immunomodulators	63/161 (39.1%)	37/107 (34.6%)	65/150 (43.3%)	29/70 (41.4%)
IBD intestinal resection	24/163 (14.7%)	37/123 (30.1%)	24/155 (15.5%)	6/74 (8.1%)
IBD colonic resection <sup>a</sup>	15/137 (10.9%)	22/93 (23.7%)	20/140 (14.3%)	4/65 (6.2%)
Colonic dysplasia <sup>a</sup>	5/111 (4.5%)	8/69 (11.6%)	5/133 (3.8%)	2/58 (3.4%)
IBD arthropathy	32/136 (23.5%)	29/104 (27.9%)	36/139 (25.9%)	10/66 (15.2%)
Dermatologic manifestations	8/139 (5.8%)	4/105 (3.8%)	7/142 (4.9%)	1/64 (1.6%)
Primary sclerosing cholangitis	4/147 (2.7%)	9/113 (8.0%)	4/147 (2.7%)	0/68 (0.0%)
Ulcerative colitis (n = 284) <sup>c</sup>				
Montreal E1 (proctitis)	1/61 (1.6%)	3/39 (7.7%)	6/78 (7.7%)	5/34 (14.7%)
Montreal E3 (pancolitis)	48/61 (78.7%)	31/39 (79.5%)	62/78 (79.5%)	24/34 (70.6%)
Crohn's disease (n = 241) <sup>c</sup>				
Montreal A1 (16-y-old)	11/65 (16.9%)	13/65 (20.0%)	8/67 (11.9%)	5/32 (15.6%)
Montreal A3 (>40-y-old)	9/65 (13.8%)	6/65 (9.2%)	20/67 (29.9%)	6/32 (18.8%)
Montreal L1 (ileal)	11/53 (20.8%)	8/47 (17.0%)	8/62 (12.9%)	7/31 (22.6%)
Montreal L2 (colonic)	11/53 (20.8%)	14/47 (29.8%)	20/62 (32.3%)	7/31 (22.6%)
Montreal L3 (ileocolonic)	31/53 (58.5%)	25/47 (53.2%)	34/62 (54.8%)	17/31 (54.8%)
Montreal B1 (inflammatory) <sup>b</sup>	30/51 (58.8%)	23/46 (50.0%)	39/61 (63.9%)	19/31 (61.3%)
Montreal p (perianal modifier)	21/63 (33.3%)	23/55 (41.8%)	20/61 (32.8%)	10/30 (33.3%)

<sup>a</sup>Colonic resection and dysplasia were only analyzed for ulcerative colitis and Crohn's disease patients with colonic disease involvement.

<sup>b</sup>"Inflammatory" defined as nonstricturing, nonpenetrating disease behavior.

$n_c$  represents total denominator for each group. However, denominators for individual variables may vary based on completeness of data in medical records.

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**Table 2.**

**Inflammatory Bowel Disease Characteristics by Birth Country**

Clinical characteristics	US-born (n = 79)	Foreign-born (n = 181)
All IBD (n = 260) <sup>c</sup>		
Ulcerative colitis	36/79 (45.6%)	108/181 (59.7%)
Female	27/79 (34.2%)	73/181 (40.3%)
Age of diagnosis 16-y-old	22/88 (25.6%)	11/182 (6.0%)
Age of diagnosis 60-y-old	4/77 (5.2%)	11/179 (6.1%)
Ever used biologics	35/78 (44.9%)	47/180 (26.1%)
Ever used immunomodulators	40/78 (51.3%)	70/179 (39.1%)
IBD intestinal resection	16/76 (21.1%)	17/180 (9.4%)
IBD colonic resection <sup>a</sup>	12/61 (19.7%)	9/163 (5.5%)
Colonic dysplasia <sup>a</sup>	2/53 (3.8%)	7/147 (4.8%)
IBD arthropathy	25/72 (34.7%)	48/160 (30.0%)
Dermatologic manifestations	10/74 (13.5%)	3/161 (1.9%)
Primary sclerosing cholangitis	1/77 (1.3%)	6/167 (3.6%)
Ulcerative colitis (n = 144) <sup>c</sup>		
Montreal E1 (proctitis)	0/29 (0%)	8/89 (9.0%)
Montreal E3 (pancolitis)	24/29 (82.8%)	67/89 (75.3%)
Crohn's disease (n = 116) <sup>c</sup>		
Montreal A1 (< 16-y-old)	16/41 (39.0%)	5/73 (6.8%)
Montreal A3 (>40-y-old)	2/41 (4.9%)	23/74 (31.5%)
Montreal L1 (ileal)	6/33 (18.2%)	12/68 (17.6%)
Montreal L2 (colonic)	11/33 (33.3%)	23/68 (33.8%)
Montreal L3 (ileocolonic)	16/33 (48.5%)	33/68 (48.5%)
Montreal B1 (inflammatory) <sup>b</sup>	17/32 (53.1%)	44/65 (67.7%)
Montreal p (perianal modifier)	15/38 (39.5%)	25/69 (36.2%)

<sup>a</sup>Colonic resection and dysplasia were only analyzed for ulcerative colitis and Crohn's disease patients with colonic disease involvement.

<sup>b</sup>“Inflammatory” defined as nonstricturing, nonpenetrating disease behavior.

$c_n$  represents total denominator for each group. However, denominators for individual variables may vary based on completeness of data in medical records.

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**Table 3.**

## Countries of Origin Identified in 260 Study Subjects

Country of origin	N	Country of origin	N
Albania	1	Ireland	2
Argentina	2	Israel	5
Australia	3	Italy	4
Bahrain	1	Jamaica	3
Bangladesh	15	Macedonia	1
Barbados	2	Malaysia	2
Brazil	2	Mexico	15
Canada	3	Philippines	4
China	15	Poland	8
Columbia	2	Puerto Rico <sup>a</sup>	10
Croatia	1	Romania	1
Dominican Republic	22	Russia	3
Ecuador	4	Senegal	3
Egypt	2	Serbia	1
El Salvador	3	Slovakia	3
France	1	Sri Lanka	4
Georgia	1	Syria	1
Greece	1	Tajikistan	1
Grenada	3	Tibet	1
Guinea	2	Trinidad	5
Guyana	3	Turkey	1
Honduras	2	Ukraine	1
Hungary	1	United Kingdom	3
India	4	United States	79
Indonesia	1	Venezuela	1
Iran	1		

<sup>a</sup>While Puerto Rico is a territory of the United States, patients from Puerto Rico were classified as foreign-born in this study.