

# An International Multicenter Study of Native and Immigrant South Asian Crohn's Unveils Unique Phenotypic and Serologic Characteristics

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## INTRODUCTION AND AIM

- Crohn's disease (CD) has emerged as a global disease, with the fastest rise in incidence in Asia.
- Immigration from South Asia (SA) to the West is associated with an increased incidence of CD, particularly from the second generation.
- Studies of native SA residents suggest unique CD characteristics.
- The impact of immigration (as a reflection of early life exposure to one environment, and later life to another) on disease phenotype, behavior, and seropositivity has not been examined previously.

## MATERIAL & METHODS

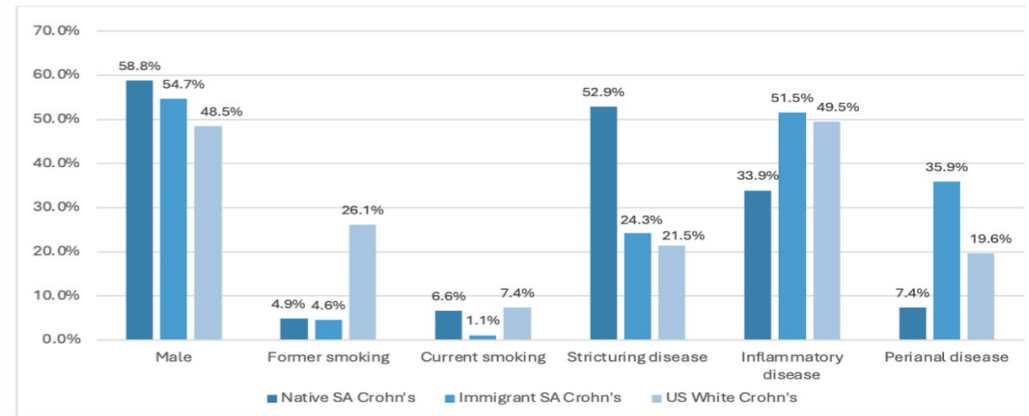
- Prospectively phenotyped a cohort of 260 US-residing (immigrant) SA-CD patients and controls from 3 US hospitals paired with 198 native SA-CD patients and controls from India and Singapore.
- These cohorts were compared to a cohort of 1679 US white CD patients.
- Detailed disease phenotype, treatment history, acculturation, environmental exposures and serologies were ascertained.

## RESULTS

- Native(59%,p=0.02) and immigrant(55%,p=0.15) SA-CD demonstrated male predominance compared to White CD patients(49%).
- Immigrant SA-CD were diagnosed at a younger age compared to native SA-CD(27.3 vs 31.7 years;p=0.02).
- 2<sup>nd</sup> generation immigrants(US-born children of SA immigrants) had a mean age of diagnosis of 17.7 years compared to 1<sup>st</sup> generation immigrants (34 years) or US white CD(27.7 years).
- Western acculturation was associated with a younger age of diagnosis (p<0.05).
- Ever smoking was uncommon in all SA-CD(native and immigrant) in contrast to white US-CD patients(9.1%vs 33.5%,p<0.0001).
- Greater frequency of stricturing (B2) behavior (52.9%) in native SA-CD compared to immigrant SA-CD(24.3%) or US-white CD(21.5%).
- 1<sup>st</sup> generation SA-CD had a higher percentage of B2 disease compared to 2<sup>nd</sup> generation SA-CD(32.3 vs 10%;p<0.001).
- Native SA-CD had a lower percentage of perianal disease(7.4%) compared to immigrant SA-CD(35.9%) and white CD(19.6%)(p<0.001).
- Immigrant SA-CD had higher proportion of anti-cbir1(48.8%) antibodies compared to ASCA positivity rate, a pattern different than historically reported in western cohorts.
- Native SA-CD patients had mostly ASCA positive(52.1%) followed by anti-cbir1(42.9%) and ANCA(10.9%).
- In both native and immigrant SA CD cohorts, seropositivity to any of the antimicrobial antibodies was uncommon in controls and greater number of anti-microbial antibodies were associated with complicated disease phenotype.

**We identified both commonalities as well as unique differences in disease phenotype, behavior, serological patterns and environmental factors by geography and immigrant status, highlighting the importance of changing environment on CD phenotypic expression**

## RESULTS



	Native South Asian Crohn's	Immigrant South Asian Crohn's	US White Crohn's	P-value
<b>Male n (%)</b>	<b>77 (58.8%)</b>	<b>58 (54.7%)</b>	<b>815 (48.5%)</b>	<b>0.0802</b>
<b>Age at Diagnosis mean±SD (IQR)</b>	<b>31.7±12 (22-40)</b>	<b>27.3 ± 14.5 (15-37)</b>	<b>27.7±14.4 (18-34)</b>	<b>&lt;.0001</b>
<b>Immune mediated disease n(%)</b>	<b>26 (20.8%)</b>	<b>30 (29.4%)</b>	<b>538 (33.1%)</b>	<b>0.0178</b>
<b>Family history of IBD n (%)</b>	<b>18 (14.2%)</b>	<b>15 (14.4%)</b>	<b>417 (25.6%)</b>	<b>0.0011</b>
<b>Bowel resection n (%)</b>	<b>2 (1.5%)</b>	<b>22 (20.8%)</b>	<b>417 (24.8%)</b>	<b>&lt;.0001</b>
<b>Biologic use n (%)</b>	<b>33 (25.8%)</b>	<b>83 (83%)</b>	<b>1061 (65.2%)</b>	<b>&lt;.0001</b>
<b>Smoking status n (%)</b>	<b>Former: 6 (4.9%) Current: 8 (6.6%)</b>	<b>Former: 4 (4.6%) Current: 1 (1.1%)</b>	<b>Former: 414(26.1%) Current: 118 (7.4%)</b>	<b>&lt;.0001</b>
<b>Ever smoker (current or former) n (%)</b>	<b>14 (11.5%)</b>	<b>5 (5.7%)</b>	<b>532 (33.5%)</b>	<b>&lt;.0001</b>
<b>Ileal disease location (L1) n (%)</b>	<b>47 (43.5%)</b>	<b>29 (29.3%)</b>	<b>325 (24.7%)</b>	<b>0.0005</b>
<b>Stricturing behavior (B2) n (%)</b>	<b>64 (52.9%)</b>	<b>25 (24.3%)</b>	<b>288 (21.5%)</b>	<b>&lt;0.0001</b>
<b>Perianal disease n (%)</b>	<b>9 (7.4%)</b>	<b>37 (35.9%)</b>	<b>314 (19.6%)</b>	<b>&lt;0.0001</b>

## SUMMARY / CONCLUSION

- Our international, multicenter study provided a comprehensive comparison between native SA-CD, immigrant SA-CD and White-CD
- We identified unique phenotype including younger age at diagnosis in 2<sup>nd</sup> generation immigrants, and more stricturing disease in native SA-CD.
- Smoking behavior was strikingly different between SA-CD(native and immigrant) and White CD patients suggesting the need to evaluate the influence of ethnicity and ancestry on this established environmental CD risk factor in Whites.
- Further larger, multicenter studies to define disease biology of CD across different ethnic populations and in different settings is a high unmet need with the globalization of CD.