Title page

Title: Emerging IBD demographics, phenotype and treatment in South-East Asia and Middle East: Preliminary findings from IBD Emerging Nations' Consortium

Short Title: IBD demographics in Southern Asia

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MAIN TEXT

Abstract

Background and aims Inflammatory bowel disease (IBD) is emerging in the newly industrialized countries of South Asia, South East Asia and the Middle East, yet epidemiological data are scarce.

Methods We performed a cross-sectional study of IBD demographics, disease phenotype and treatment across 38 centers in 15 countries of South Asia, South-East Asia and Middle East. Intergroup comparisons included gross national income(GNI) per capita.

Results Among 10,400 patients, ulcerative colitis (UC) was twice as common as Crohn's disease (CD), with a male predominance (UC 6678, CD 3495, IBD-Unclassified 227, 58% male). Peak age of onset was in the third decade, with a low proportion of elderly onset IBD (5% age >60). Familial IBD was rare (5%). The extent of UC was predominantly distal (proctitis/left sided 67%), with most being treated with mesalamine (94%), steroids (54%), or immunomodulators (31%). Ileocolic CD (43%) was commonest, with low rates of perianal disease (8%) and only 6% smokers. Diagnostic delay for CD was common (median 12 months; IQR 5-30). Treatment of CD included mesalamine, steroids and immunomodulator (61%, 51% and 56% respectively), but a fifth received empirical anti-tubercular therapy. Treatment with biologics was uncommon (4% UC,13% CD) which increased in countries with higher GNI per capita. Surgery rates were 0.1 (UC) and 2 (CD)/100 patient/years.

Conclusions The IBD-ENC cohort provides insight into IBD in South-East Asia and the Middle East, but is not yet population-based. UC is twice as common as CD, familial disease uncommon and rates of surgery are low. Biologic use correlates with per capita GNI.

Keywords: Inflammatory bowel disease, South Asia, South-East Asia, Middle East, IBD ENC

1. **Introduction**

Inflammatory bowel disease (IBD) is a common disease in Western (predominantly Caucasian) populations, including Europe and the USA. The past two decades have seen IBD

emerge in the previously low incidence regions of South and South east Asia including the middle east.[1-5]

IBD in these countries appears to share some common features, despite vast geographical and economic diversity. IBD is emerging rapidly in these areas, irrespective of socio-economic status or rural-urban divide,[3-6] with similar challenges in diagnosis and management. Differentiating IBD from infectious disease particularly tuberculosis dominates decision-making,.[7-8] High population density, together with low resources affect access to healthcare, The cost of chronic disease management has a major impact on budgets traditionally focused on short term, infectious disease.[7-9] As IBD emerges, there is a need to understand the disease of the region and reconcile the most appropriate strategies for patient management from the perspectives of cost, efficacy of treatment and long term care. There is very limited data on the nature and phenotype of IBD in this region . Most of these countries do not have a national IBD registry nor dedicated IBD centers.[2] Variations in disease phenotype may help to identify genetic, environmental, or dietary factors contributing to IBD.[11-12].

The primary aim of this study was a cross sectional survey to identify clinical demographics and phenotypes of IBD in 15 countries across South Asia, South-East Asia and the Middle East. We also aimed to compare differences in management between the member countries based on Gross national income (GNI) per capita.

2. Methods

The IBD Emerging Nations' Consortium (IBD-ENC) was founded in 2015 including countries across South Asia, South-East Asia and the Middle East where IBD was emerging.[2] The objectives of the collaboration are to:

a) describe baseline demographics and the phenotypes of IBD in this geographical region
b) foster a network for research collaboration, and
c) increase understanding of IBD in challenging socioeconomic environments.

All members in the IBD-ENC are gastroenterologists with a special interest in IBD. Centers were selected based on ability to recruit patients with IBD and to collect patient data.

2.1 Study population

The study involved patients from 38 centers in 15 countries across South-East Asia and the Middle East including Afghanistan, Bangladesh, Egypt, India, Indonesia, Kuwait, Malaysia, Myanmar, Nepal, Philippines, Qatar, Sri Lanka, Thailand, United Arab Emirates (UAE), and Vietnam (Figure 1A) (Supplementary table 1). A standardised proforma was distributed in February 2017 to participating gastroenterologists for data collection. Patients, whether outpatients or inpatients, were identified prospectively at each center and the proforma completed

2.2 Patient data collection and ethical consideration

A standardized proforma comprising patient demographics, phenotype and treatment details were used for data collection. This included age and sex, age at onset of symptoms and at IBD diagnosis (to calculate diagnostic delay), educational and occupational status, smoking history, history of appendectomy prior to diagnosis, family history of IBD, history of tuberculosis, disease extent and phenotype (based on Montreal classification)[15], extra-intestinal manifestations and details of drug treatment or surgery for IBD. Data collection was performed at each center between June 2017 and November 2018. The completed dataset from individual members were collated for further analysis.

2.2 Case definitions

The diagnosis of UC or CD or indeterminate was based on symptoms, endoscopy, radiology and histopathological findings consistent with a diagnosis of IBD.[13,14] The Montreal classification was used to characterize disease location and behavior.[15] We included patients with a confirmed diagnosis for more than 6 months to exclude infectious mimics of IBD including intestinal tuberculosis. Cases where the diagnosis remained uncertain were excluded.

2.4 Comparison within the cohort based on gross national income (GNI) per capita (Figure 1B) : The IBD-ENC countries were subdivided into 4 groups based on GNI per capita:

- low income countries (GNI per capita <1025 USD; Afghanistan and Nepal)
- lower middle income countries (GNI per capita 1026-3995 USD; India, Bangladesh, Myanmar, Vietnam, Philippines, Indonesia, Egypt)
- upper middle income countries (GNI per capita 3996-12375; Malaysia, Thailand, Sri Lanka), and
- high income countries (GNI per capita >12376 USD; Kuwait, Qatar, UAE).[16]

The disease demographics, disease phenotype and treatment pattern was compared amongst the groups.

2.5 Comparison with Western and other Asian cohorts

Two cohorts from Europe and Asia were selected for broad comparison, although not for statistical analysis. The Epidemiology Committee (EpiCom) cohort of the European Crohn's Colitis Organization (ECCO), a was the Western (Caucasian) cohort.[17,18] The Asian subgroup of the Asia-Pacific Crohn's and Colitis Epidemiological Study (ACCESS) was the comparator for an East-Asian population with different ethnicity.[19,20] . Disease location/phenotype were compared at diagnosis, and treatment at the time of maximum follow up, owing to variable follow up duration.[18, 20]

2.6 Data analysis

Data was tabulated in Microsoft Excel. Descriptive statistics included percentages rounded to the nearest whole number, based on valid data per parameter, excluding patients with missing values. Quantitative data presented as mean (± standard deviation [SD]) for data with normal distribution and median (interquartile range-IQR) for skewed distribution. Categorical variables, compared using chi-square test or Fischer's exact test; And Continuous data using Student's 't' test or Mann-Whitney-U test, MedCalc version 19.2.1.was used for the statistical analysis. A p-value of < 0.05 was considered statistically significant.

3. Ethical considerations

All patients provided informed consent prior to data collection, which was anonymised. The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethics committee of the institutions (AIG/IEC31/05.2018-02/ER).

4. Results

4.1 Demographics

Of 10,935 patients.535/10935 (5%) with incomplete data were excluded from the analysis. 10400 patients (UC n=6678,64%; CD n=3495, 34%; IBD unclassified n=227, 2%) were included. The unadjusted UC:CD ratio was 1.9:1 (Table 1, supplementary table 2A). There was large geographic variation. northern India (ratio 16:1) and Myanmar (ratio 124:1). UAE reported more CD than UC (UC:CD 0.8). The median duration of follow up for prevalent cases was 91 months (IQR- 55-154 months, range- 6-630 months).

The overall male:female ratio in the entire cohort was 1.37:1 (UC 1.3; CD 1.4), with a modest male preponderance (male n= 6013/10400, 58%). Most countries had a male:female ratio >1, most strikingly in Afghanistan (72%) and Kuwait (79%). The male:female ratio was ≤1 in Thailand, Myanmar, Vietnam and Sri Lanka.

The median age of onset of UC was 35 years (IQR 26-46, range 4-84) and CD 31 years(IQR- 22-42, range 4-83 yrs). There was no bimodal distribution of age of disease onset. Elderly onset IBD (>60 years) was reported in 5% of cases.

4.2 Disease phenotype and behavior

The overall distribution of UC (n=6678/10400) at diagnosis was proctitis (E1, n=1803, 27%), left sided colitis (E2, n=2689, 40%) and extensive colitis (E3, n=2186, 33%) (Figure 2) (See Supplementary Figure 1 and Table 2 for countrywide distribution).

The distribution of CD at diagnosis (n=3495/10400) was ileal (L1, n=951, 27%), colonic (L2, n=937, 27%), ileocolic (L3, n=1505, 43%) and upper GI (L4, n=160, 5%) (Figure 2).(Table 3). Peri-anal disease (p) was reported in 8% (n=291/3495) (Figure 2).

The behaviour of CD was inflammatory (B1, n=2231, 64%), stricturing (B2, n=819, 23%), or penetrating (B3, n=383, 11%), at the time of data collection (median follow up 91 months) . There was some heterogeneity within IBD-ENC, with UAE reporting a high frequency of stricturing (B2) disease (n=41/68, 60%).

4.3 Extra-intestinal manifestations (EIMs)

Overall, EIMs were reported in 2007/9174 (22%) patients: arthropathy in 1646/9174 (18%: peripheral, 1467/9174 (16%); axial 179/9174 (2%)); cutaneous: 491/9174 (5%); ocular :285/9174 (3%) and primary sclerosing cholangitis (PSC) :44/9174 (0.5 % of total, of which most (69%) had UC). (Supplementary table 3).

4.4 Occupational and educational status

Data of 7966 patients available 5387(68%) employed;1288 (16%) students; 756 (9%) homemakers, and 248 (3%) retired. 287(4%) were unemployed due to IBD

Educational status available for 7123 patients, 2920(41%) completed secondary (High School) level; 3968 (56%) tertiary (University) level; 235 (3%) patients had no formal education. (Supplementary table 2B).

4.5 Family history of IBD

A family history (any first or second degree relative) with IBD was noted in only 5% (390/8429, 4% for UC, 7% for CD and 2% for IBD-U). Among familial IBD, first degree relatives were affected in 3% (242/8429) cases. (Supplementary table 2C).

4.6 IBD and smoking

Around 6% patients (566/9506; 329UC; 292 CD) were smokers and 5% (508/9506) were ex-smokers. (Supplementary table 2C).

4.7 Diagnostic delay

Diagnostic delay data was available in 3346 patients across 11 countries. The median delay from the onset of symptoms to diagnosis was 10 months (IQR 3-24, range 1-121 months). The diagnostic delays in UC (median 6 mo, IQR-2-15) was significantly shorter than CD (median 12 mo, IQR-5-30) ($p < 0.0001$- Mann Whitney U test).

4.8 Prior history of appendectomy

A history of appendectomy was noted in 1% UC (72/5893) and 4 % (131/3078) CD. (Supplementary table 2C).

4.9 Empirical anti-tubercular therapy

A therapeutic trial of anti-tubercular therapy was used primarily in CD**:** 588 of 3063 (19%) and 107/5712 (2%) with UC received empirical anti-tubercular therapy. The use of empirical therapy was highest in Bangladesh (32%) followed by India (25%), Thailand (11%) and Nepal (8%) (Supplementary Figure 2). Data on the same was not available from Qatar or Vietnam. Countries with only few CD cases (Afghanistan, Kuwait, Myanmar and Egypt) did not have patients on empirical anti-tubercular therapy.

4.10 Treatment used

For UC, drugs prescribed at the time of data entry were mesalamine (6283/6678; 94%), corticosteroids (3584/6678, 54%), immunomodulators (2086/6678, 31%) and biological therapy (267/6678, 4%). Topical therapy (mesalamine or steroid enema) was used in

(1467, 22%). Therapy for CD included mesalamine (2124/3495, 61%), steroids (1776/3495, 51%), immunomodulators (1966/3495, 56%) and biological therapy (469/3495, 13%) (Figure 2).Overall, biologic therapy was used in 7% (736/10400) IBD patients. The countries with the highest biologic usage were Kuwait (50%), UAE (46%), Egypt (37%), Philippines (37%) and Qatar (24%). No biological therapy was prescribed in Afghanistan, Myanmar, Indonesia, or Vietnam (Table 2 and 3). There was wide variation in biologic usage, even among countries with a high GNI/capita (Figure 2).

4.11 Surgery rates in UC and CD

At the time of data collection, 92/6678 (1%) patients with UC had undergone colectomy; 613/3495 (17%) patients with CD had undergone intestinal surgery, with a median follow up of 95 months (range 6-639 months) and 90 months (range-6-622 months) respectively. The rate of colectomy in UC was 0.1 per 100 UC patients per year and intestinal surgery rate in CD was 2 per 100 CD patients per year. Prior to surgery, 12% (11/92) UC and 13% (80/613) CD patients had received biologics and 51% (47/92) UC and 64% (392/613) CD received immunomodulators.

4.12 Comparison among member countries based on Gross national income (GNI) per capita (Figure 2) : [6] Among demographic factors, there was a decrease in the UC:CD ratio from low income to high income countries (2.2 in low income, 1.5 high income) (Supplementary table 4). There was no major difference in clinical phenotype among these groups,.

There were, however, differences in therapy. For UC, more patients received immunomodulator (38%) or biologic therapy (15%) in high and upper middle income groups, compared to 15% immunomodulators ($p<0.00001$) and 0% (biologics, $p=0.0001$) in low income countries. Steroid usage was significantly higher from low income (73%) compared to high income (55%, $p=0.0004$) s. Although treatment patterns differed, colectomy rates were similar in all groups.

For CD, high income countries reported higher biologic usage compared to low income countries (45% vs 2%, p<0.0001), higher immunomodulator usage (66% vs 48%) (p=0.014), higher surgery rates (p=0.009) and a lower rate of empirical anti-tubercular therapy (p=0.0002). Biologic usage progressively increased from low income to high-income group in both UC and CD (Supplementary table 5 and 6).

4.13 Broad comparison with Western (EpiCom) and Asian (ACCESS) cohorts (Figure 3) The proportion of pancolitis (E3) in UC were similar in all three cohorts. Left sided colitis was most common in IBD-ENC(40%) and Epicom (47%); Proctitis in ACCESS (37%).
In CD, ileocolic disease was most common (43%) in IBD-ENC and ACCESS cohort (49%). Ileal disease commonest in EpiCom 46%. 8% IBD-ENC had perianal disease, compared to 18%(ACCESS) and 12% (EpiCom). 22% reported extra-intestinal manifestations in IBD-ENC, compared to EpiCom (11%) and ACCESS (18% in Asian subgroup). Biologic use was limited in IBD-ENC, (4%UC and 13% CD) compared to the other two cohorts. Colectomy rates in UC were low in IBD- ENC (1% over median follow up of 9 years) compared to ACCESS (2% at 1year) and EpiCom (4% at 5yrs). All these comparisons are tenuous, since data collection methods differed and IBD-ENC was not population-based.

5. Discussion

The IBD ENC cohort included more than 10000 patients across 15 countries of South-East Asia and the Middle East, where IBD is an emerging disease. IBD in South Asian patients remains “under-appreciated and understudied” as reported by Kochar et al in 2020.[21] Ours is the first paper to describe cross sectional demographics and phenotype of IBD in the South and South-East Asia ‘geographic belt’, which predominantly consists of newly industrialized nations with emerging economies (Fig 1). In many of these countries, including Af-

ghanistan, Myanmar, Nepal and Vietnam, there are no previous data on the clinical epidemiology, demography, or phenotype of IBD.[2,4] The region is highly populous and the increasing incidence of IBD represents a major proportion of the global burden of IBD. The data, therefore, reflect the nature of IBD in an area where IBD is emerging, a large region facing similar challenges in diagnosis and management (table 4).[7]

Understanding the epidemiology of an emerging disease in this part of the world has important implications. First of all, it characterizes the disease phenotype, highlights the challenges of diagnosis and management unique to the region and paves the way for modifying management algorithms.[7] Secondly, estimation of the disease burden is essential for healthcare policymakers. This in turn results in increased awareness of IBD for the public, health care professionals and governing bodies. This matters, because most of the countries included in IBD-ENC do not consider IBD as a public health problem. Finally, it also provides an opportunity to monitor the evolution of this chronic disease and identify potential environmental triggers contributing to the emergence of this disease.[11-12]

We found the prevalence of UC to be approximately double that of CD. This is consistent with previous data from populations where IBD is emerging.[4] In countries such as Afghanistan, Bangladesh and Myanmar, the UC: CD ratio was substantially above 3:1. South India reported a lower ratio than northern India. The large difference is likely to be real,[22] indicating different exposure to unknown environmental factors[7]and Increasing urbanisation.[4] Overall, there was a male preponderance in IBD, in contrast to a slight female preponderance of IBD in Western cohorts.[23] This may reflect more migration of menfolk to industrialized areas for education or job seeking,[10] fewer women accessing health care, and gender inequality among poorer socio-economic groups. The male:female ratio was reversed in Myanmar, Thailand and Vietnam with a matriarchal society or a large female work force,[24].

The overwhelming male preponderance in Afghanistan (72%) is probably because females are reluctant to undergo colonoscopy due to sociocultural barriers. The relatively low proportion of older patients (<5% age >60 years) is a notable difference to the West.[25] Similarly the number of active smokers in our study was low CD(7%), or UC(6%) compared to western cohorts.[10]

Another notable difference between our cohort and Western cohorts include the lack of familial aggregation (Supplementary Table 2C).[26] This is, however, consistent with other Asian studies.[27,28] A study of Indian patients found familial IBD was associated with a higher frequency of ulcerative pancolitis and fistulizing CD.[29] The same association was not evident in IBD-ENC, with similar rates of pancolitis in both familial and sporadic UC (32% versus 31%). Perianal disease was uncommon in IBDENC (8%). This contrasts to reported rates of perianal disease of 30-58% in Asian studies from Japan, China and Hong Kong.[30-32]

The diagnostic dilemma between CD and intestinal TBAnd the consequent use of empirical anti-tubercular therapy is unique to IBD in this region.[33-35] 19% CD patients received empirical anti-tubercular therapy before diagnosis contributing to inordinate diagnostic delays.[36,37] Diagnostic delays worsen outcomes, with increased complications and need for surgery.[38] The higher rate of surgery in CD in our cohort could also be related to the delayed diagnosis.

Treatment of IBD in the IBD-ENC cohort was much as expected. Mesalamine and steroids were the mainstay of treatment. Oral mesalamine was still used in two-thirds of patients with CD, despite Asia Pacific guidelines stating the ineffectiveness of mesalazine for inducing remission.[39,40] The practice could be related to the general safety of aminosalicylates, compared to immunomodulators, as well as availability and affordability of the drugs.

Immunomodulator use was comparable to studies from Western and Asian cohorts in both UC and CD.17-20 Azathioprine was unavailable in Afghanistan. Again, Afghanistan, Myanmar and Vietnam did not have access to biologic therapy. This highlights the great disparity in drug availability among IBD-ENC countries, with a very low use of biologics (Figure 2).41,42 Additionally high cost, lack of insurance and the prevalence of infections and tuberculosis preclude biologic use in this region,.9

The overall biologic usage in our cohort was around 6.7%. Within IBD-ENC, the low and lower middle income countries had significantly lower biologic usage compared to the higher income countries. Compare this with Japan, where 30-40% of CD receive biologic therapy and almost all expenses of IBD treatment are borne by the government.[41,43,44] Despite limited biologic usage, the colectomy rate for UC was low (0.1 per 100 UC patients per year). A decline in colectomy rates after introduction of anti-TNF therapy to 0.9 per 100 UC patients per year has been reported in a study from Canada, but was still appreciably higher than our cohort.[45] However the intestinal surgery rates for CD (2 per 100 patients per year) was higher than Western studies in the post-biologic era (0.4-0.8%).[46,47]

Despite its novelty, there are clear limitations to the study. It was cross-sectional, not population-based nor an inception cohort. The number of cases varied greatly among countries. Most sites were secondary or tertiary care centers, which introduces selection bias, not reflective of the general population. The low resource settings of the region are likely to have influenced results, since many IBD-ENC countries lack adequate diagnostic facilities, including colonoscopy or GI pathology services. There is limited awareness of IBD and very few dedicated IBD centers. The cumulative probability of an outcome (such as time to initiation of IBD therapy, surgery, or change in disease phenotype) could not be evaluated

with the cross-sectional data. Comparisons with Western and Asian data are at best tentative as a consequence.

6. Conclusions

Despite these limitations, the IBD-ENC study is a first insight into the nature of IBD, its demographics and phenotype from countries that include Afghanistan, Myanmar, Nepal and Vietnam. It includes a cohort of more than 10000 patients from 15 countries in the same geographic belt, where epidemiological data on IBD are few or unreported. It represents a step towards future research in understanding the environmental factors in countries where the diseases are emerging. We found UC was twice as common as CD in the region. The extent of UC was similar to other cohorts, although colectomy rates were very low. Inflammatory, ileocolic CD (B1/L3 phenotype) was the dominant pattern of CD, with a low frequency of perianal disease and surgery, despite appreciable diagnostic delay. Our data provide a baseline and represent a step towards future research in understanding disease behavior of IBD from countries where the diseases are emerging.

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Table 1. Demographic characteristics and extra intestinal manifestations of Inflammatory Bowel Disease (IBD) patients in IBD- Emerging Nations’ Consortium (IBD- ENC) cohort

Demographic variables	N (Percentage)
Male	6013 (58%)
UC	6678 (64%)
CD	3495 (34%)
IBD-U	227 (2%)
UC: CD	1.9:1
Education (data available n= 7123)	
No education	235 (3%)
Primary/secondary	2920 (41%)
Tertiary	3968 (56%)
Employment status (data available, n=7966)	
Unemployed	287 (4%)
Employed	4306 (54%)
Self employed	1081 (14%)
Student	1288 (16%)
Retired	248 (3%)
Housewife	756 (9%)
Smoking status (available data - 9506)	
Current smoker	566 (6%)
Former smoker	505 (6%)
Non-Smoker	8435 (89%)
Appendectomy (available data, n=8954)	
Appendectomy	203 (2.3%)
Family history, (available data, n=8429)	
Family history	390 (4.6%)
First degree relative	242 (2.9%)
Extra-intestinal manifestations (available data, n=9174)	
Total EIM	2007 (22%)
Eye	285
Peripheral joints	1467
Skin	492

Ankylosing spondylitis	179
PSC	44

Table 2. Disease phenotype and treatment of ulcerative colitis (UC) (TB- Tuberculosis, 5-ASA- 5-amino-salicylic acid)

Characteristic, n (%)	UC	E1 (proctitis)	E2 (left sided colitis)	E3 (Extensive colitis)	5-ASA	Steroids	Immunomodulators	Biologics	anti-TB therapy	Surgery
All patients	6678	1803	2689	2186	6283	3584	2086	267	107	92
		27%	40%	33%	94%	54%	31%	4%	1.9%	1%
Afghanistan (n)	22	3	14	5	21	20	0	0	2	0
%		14%	64%	23%	95.0%	91.0%	0%	0%	9.0%	0%
Bangladesh (n)	432	85	167	180	411	349	76	7	10	1
%		20%	39%	42%	95%	81%	18%	2%	2%	0%
Egypt (n)	38	12	14	12	38	36	26	15	0	3
%		32%	36%	32%	100%	95%	68%	39%	0%	8%
North India (n)	728	175	272	281	609	381	165	1	4/454	7
%		24%	37%	39%	84%	52%	23%	0%	1%	1%
South India (n)	2515	475	1263	777	2418	1007	881	46	35	26

%		19%	50%	31%	96%	40%	35%	2%	1%	1%
West India (n)	551	200	140	211	523	380	106	24	47	11
%		36.3%	25.4%	38.3%	95%	69%	19%	4%	9%	2%
Indonesia (n)	27	5	7	15	23	6	1	0	1	0
%		19%	25%	56%	85%	22%	4%	0%	4%	0%
Kuwait (n)	12	3	3	6	12	11	2	6	0	0
%		25%	25%	50%	100%	92%	17%	50%	0%	0%
Malaysia (n)	553	356	52	145	519	166	197	47	2	10
%		64.3%	9.4%	26.3%	94%	30%	36%	8%	0%	2%
Myanmar (n)	248	91	55	102	244	211	16	0	3	1
%		37%	22%	41%	98%	85%	6%	0%	1%	0%
Nepal (n)	79	35	25	19	75	54	15	0	0	2
%		44%	32%	24%	95%	68%	19%	0%	0%	3%
Phillipines (n)	25	5	13	7	21	20	10	8	0	4
%		20%	52%	28%	84%	80%	40%	32%	0%	16%
Qatar (n)	552	142	268	142	544	282	198	72	NA	10
%		26%	48%	26%	99%	51%	36%	13%	-	2%
Srilanka (n)	473	141	211	121	421	393	229	16	1/333	9
%		28%	46%	26%	89%	83%	48%	3%	0%	2%
UAE (n)	56	5	31	20	44	45	33	17	0	1

%		9%	55%	36%	79%	80%	59%	30%	0%	2%
Vietnam (n)	107	10	62	35	107	59	0	4	NA	0
%		9%	58%	33%	100%	55%	0%	4%		0%
Thailand (n)	260	60	92	108	253	164	131	4	2	7
%		23%	35%	42%	97%	63%	50%	2%	1%	3%

Table 3. Disease phenotype and treatment of Crohn's disease (TB- Tuberculosis, 5-ASA-5-amino-salicylic acid)

Characteristic, n (%)	**Crohn's Disease**	**L1 (Ileal)**	**L2 (colonic)**	**L3(Ileo-colonic)**	**L4(upper GI)**	**B1 (Inflmmatory)**	**B2 (Stricturing)**	**B3 (Fistulizing)**	**P (perianal)**	**5-ASA**	**Steroids**	**Immunomodulators**	**Biologics**	**Anti-TB therapy**	**Surgery**
All patients	3495	951	937	1505	160	2231	819	383	291	2124	1776	1966	469	588/3063	613
%		27%	27%	43%	5%	64%	23%	11%	8%	61%	51%	56%	13%	19%	18%
Afghanistan	7	1	5	1	0	5	1	1	0	7	6	0	0	0	0
%		14%	71%	14%	0%	71%	14%	14%	0%	100%	86%	0%	0%	0%	0%
Bangladesh	101	23	15	59	4	54	35	11	3	76	83	39	1	32	35
%		22%	15%	58%	4%	53%	35%	11%	3%	75%	82%	39%	1%	32%	35%
Egypt	37	19	3	14	6	27	4	6	4	20	34	35	13	0	2
%		51%	8%	38%	16%	73%	11%	16%	11%	54%	92%	95%	35%	0%	5%

North India	45	21	3	21	2	16	15	13	10	29	21	31	0	15	18
%		47%	7%	47%	4%	36%	33%	29%	22%	64%	47%	69%	0%	33%	40%
South India	1842	481	444	834	83	1211	409	171	91	1180	812	933	122	452	293
%		26%	24%	45%	5%	66%	22%	9%	5%	64%	44%	51%	7%	25%	16%
West India	216	85	91	40	2	137	46	24	35	199	148	67	26	52	47
%		39%	42%	19%	1%	63%	21%	11%	16%	92%	69%	31%	12%	24%	22%
Indone-sia	17	2	11	4	1	13	1	1	1	15	5	3	0	1	1
		12%	65%	24%	6%	76%	6%	6%	6%	88%	29%	18%	0%	6%	6%
Kuwait	2	0	2	0	0	1	0	1	0	1	2	0	1	0	0
%		0%	100%	0%	0%	50%	0%	50%	0%	50%	100%	0%	50%	0%	0%
Malay-sia	303	60	142	92	9	174	81	47	16	156	80	216	68	3	19
%		20%	47%	30%	3%	57%	27%	16%	5%	51%	26%	71%	22%	1%	6%
Myan-mar	2	0	1	1	0	2	0	0	0	2	1	1	0	0	0
%		0%	50%	50%	0%	100%	0%	0%	0%	100%	50%	50%	0%	0%	0%
Nepal	39	17	1	20	3	31	7	1	2	19	28	22	1	3	2
%		44%	3%	51%	8%	79%	18%	3%	5%	49%	72%	56%	3%	8%	5%
Phil-lipines	22	3	11	7	1	15	5	3	4	16	12	8	6	1	10
%		14%	50%	32%	5%	68%	23%	14%	18%	73%	55%	36%	27%	5%	45%

Qatar	345	104	49	192	12	169	137	39	23	125	110	220	147	NA	69
%		30%	14%	56%	3%	49%	40%	11%	7%	36%	32%	64%	43%	NA	20%
Srilanka	237	48	87	102	15	185	20	32	58	110	202	184	20	7/177	41
%		20%	37%	43%	6%	78%	8%	14%	24%	46%	85%	78%	8%	4%	17%
UAE	68	24	5	36	3	41	22	7	12	1	61	54	40	2	14
%		35%	7%	53%	4%	60%	32%	10%	18%	1%	90%	79%	59%	3%	21%
Vi-etnam	27	2	13	12	2	20	6	1	3	27	22	0	0	NA	1
%		7%	48%	44%	7%	74%	22%	4%	11%	100%	81%	0%	0%	NA	4%
Thai-land	185	61	54	70	17	130	30	25	29	141	149	153	24	20	61
%		33%	29%	38%	9.00 %	70%	16%	14%	16%	76%	81%	83%	13%	11%	33%

Table 4. Challenges in diagnosis and management of Inflammatory Bowel Disease (IBD) in the IBD Emerging Nations' Consortium (IBD-ENC) countries

COUNTRY	**National IBD registry/pro-spective data-base availa-ble?**	**Healthcare ex-penditure per capita (USD) 2017 esti-mate**	**TB incidence per 1 lac pop-ulation per year (2017 esti-mate)**	**Diagnostic delay (me-dian and IQR) (months)**	**Rural co-lonos-copy?**	**Biolog-ics availa-ble?**	**Drug cost reimburse-ment avail-able?**	**Paediatric IBD spe-cialist availa-ble?**
Afghani-stan	No	67.12	100-199	6 (3-15.6)	No	No	No	No
Bangladesh	No	36.28	200-299	16 (8-36)	No	Yes	No	No

Egypt	No	105.77	0-24	12 (7-24)		Yes	Yes (in the government sector)	No
India	No	69.29	200-299	23 (13-48)	No	Yes	Personal insurance	Yes
Kuwait	No	1529.08	25-99	4 (3-6)	No/Not applicable	Yes	Only for nationals not for expats	YEs
Indonesia	No	114.97	≥ 300	5 (3-14.8)	No	Yes	Yes (limited for biologics)	No
Malaysia	National retrospective database (but incomplete)	384.07	25-99	13 (10-52)	Yes	Yes	Yes (but limited especially for biologics)	Yes (limited)
Myanmar	No	58.04	≥ 300	11 (5-24)	No	No	Partial	No
Nepal	No	47.92	100-199	16 (6-52)	No	Yes	No	No
Philippines	No	132.90	≥ 300	13 (5-43)	Yes	Yes	Personal insurance	Yes
Qatar	In process of being developed	1649.19	0-24	9 (4-40)	No	Yes	Yes through multiple schemes	Yes
Srilanka	No	159.48	25-99	15 (6-36)	Yes	Yes	Yes (provided free at state hospitals)	Yes (limited)
Thailand	No	247.04	100-199	12(8.5-48.5)	Yes	Yes	Yes (government employee and personal insurance	Yes

UAE	Ongoing	1357.02	0-24	6.5 (4-10)	Yes	Yes	Yes	Yes (limited)
Vietnam	No	129.58	100-199	13 (6-34.75)	No	Yes	Yes	Yes (limited)

Supplementary table 1. Name and settings of different centres involved in Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) study

Supplementary table 2. Demographic features of Inflammatory Bowel Disease (IBD) patients in IBD- Emerging Nations' Consortium (IBD- ENC) countries. A. Sex, type of disease, B. Education, occupation, C. Smoking status, appendectomy, family history.

Supplementary table 3. Extra-intestinal manifestations of Inflammatory Bowel Disease (IBD) patients in IBD- Emerging Nations' Consortium (IBD- ENC) countries.

Supplementary table 4. Demographic features of Inflammatory Bowel Disease (IBD) patients in IBD- Emerging Nations' Consortium (IBD- ENC) countries subdivided based on gross national income (GNI) per capita

Supplementary table 5. Disease phenotype and treatment of ulcerative colitis (UC) in Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) countries subdivided based on gross national income (GNI) per capita (TB-tuberculosis)

Supplementary table 6. Disease phenotype and treatment of Crohn's disease in Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) countries subdivided based on gross national income (GNI) per capita (5-ASA: 5-amino-salicylic acid)

Figure legends

Figure 1. A**.** Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) member countries, B. IBD-ENC countries based on gross national income (GNI) per capita

Figure 2 Comparative analysis of Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) study and its subgroups divided based on gross national income (GNI) per capita in united states dollars (USD): low income countries (GNI per capita <1025 USD), lower middle income countries (GNI per capita 1026-3995 USD), upper middle income countries (GNI per capita 3996-12375) and high income countries (GNI per capita >12376 USD). A) Disease extent: Ulcerative colitis (UC); B) Disease Extent: CD (C). Disease behaviour: CD; D) Treatment modalities: UC and CD

Figure 3 Comparative analysis of Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) study, Asia-Pacific Crohn's and Colitis Epidemiology Study (ACCESS)- Asian subgroup, Epidemiological Committee (Epi-Com) study - West European subgroup A) Disease extent: Ulcerative colitis (UC); B) Disease Extent : CD (C). Disease behavior: CD; D) Treatment modalities: UC and CD

Supplementary Figure 1. Bar diagrams showing disease extent for ulcerative colitis (UC) in member countries of Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD-ENC) study group. UAE- United Arab Emirates

Supplementary Figure 2. Bar diagram showing percentage of Crohn's disease (CD) patients with history of empirical anti-tubercular therapy prior to diagnosis of CD across different Inflammatory Bowel Disease- Emerging Nations' Consortium (IBD- ENC) member countries (countries with available data on anti-TB therapy and more than 10 CD patients are included)