

Crohn's disease in South Asia

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Abstract – Crohn's disease (CD) is a highly complex disease of unknown aetiology. We analysed the epidemiology, clinical characteristics, diagnosis, treatment and pathogenesis of Crohn's disease in South Asia compared to the rest of the world.

The PubMed database and Google scholar were searched till March 2016 for articles on CD. Articles dealing with CD in South Asians were reviewed by the authors, critically analysed and then summarized.

There is a lower incidence of CD in South Asia compared to the West and disease characteristics differ. Although novel genetic factors associated with CD have been identified, significant gaps exist in relation to disease pathogenesis, molecular genetic mechanisms and the use of evidence based treatment modalities.

Our review provides a comprehensive overview of existing knowledge on CD in South Asia and identifies gaps in knowledge for future research.

Keywords – Crohn's Disease; South Asia; Epidemiology; Genetics; Clinical Features; Treatment.

I. INTRODUCTION

Inflammatory Bowel Disease (IBD) has historically been regarded as a disease primarily occurring in the Western countries. However, recent studies from several Asian countries points to an increasing incidence in this part of the world [1]. The reasons for this increase are thought to be multifactorial, and may include economic development and prosperity, changes in life style and genetic factors [2]. Inflammatory bowel disease, particularly Crohn's disease (CD) is a highly complex disorder of unknown aetiology. Several factors such as genetic susceptibility, environmental factors and host immune response may play a role in its pathogenesis [3]. South Asia is a densely populated region in the world with populations comprising of different race, culture, genetic makeup, lifestyle and dietary habits. We reviewed the epidemiology, clinical characteristics, pathogenesis, diagnosis and treatment of CD in South Asia.

II. METHODOLOGY

A bibliographic search of relevant studies published in English before March 2016 was done in PubMed and Google Scholar. The following key words were used in the search: Crohn's disease, inflammatory bowel disease, South Asia, developing country, epidemiology, clinical

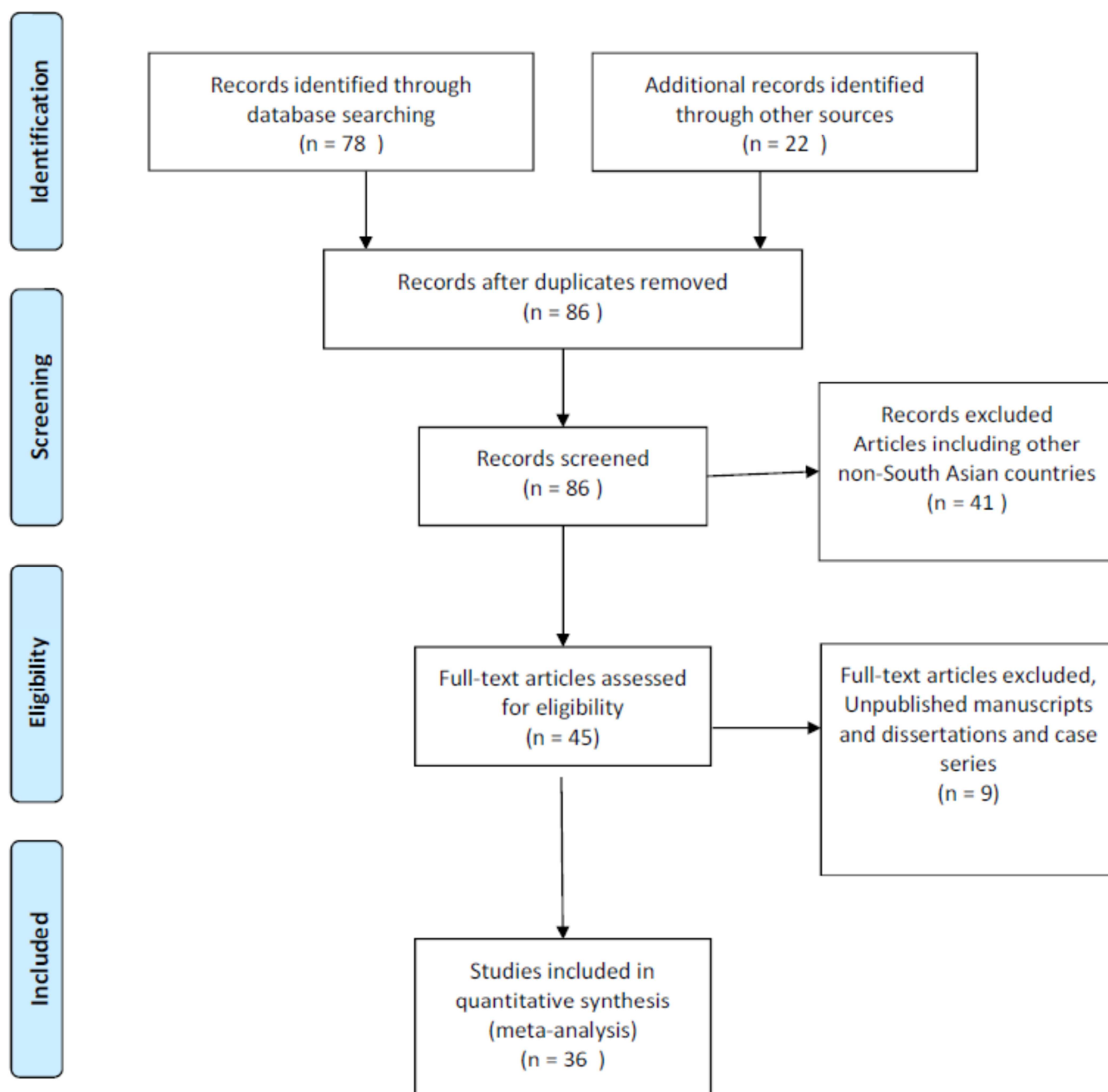
characteristics and genetics. The "related articles" function was used to expand the literature search. Initially, the article titles and abstracts were screened for relevance and then, full-text articles were manually retrieved to conduct a more detailed search. Unpublished manuscripts and dissertations were not included in this review. The retrieved articles were reviewed by the authors and studies of CD in South Asia populations were critically analysed. The Prisma flow chart outlines our selection scheme. The collected information were analysed and summarised under several headings.

A. EPIDEMIOLOGY OF CD IN SOUTH ASIA

Only two studies (both from Sri Lanka) have assessed the prevalence and incidence of CD in a South Asian country. In the first, a hospital based prevalence and incidence study was conducted in two districts (out of 9) in Sri Lanka [3]. The Gampaha and Colombo districts have a combined population of 4.5 million and the prevalence and incidence of CD were 1.2 and 0.09 per 100,000 respectively [3] (Table 1 [3, 4]) The incidence of CD was lower than that of Ulcerative colitis (UC) which was 5.3 per 100,000. As this was a hospital based study, it is possible the prevalence and incidence rates of CD may have been under-estimated, as a sizeable proportion of patients seek care from



PRISMA Flow Diagram



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TABLE 1: SUMMARY OF PREVALENCE STUDIES OF CD IN SOUTH ASIA

Country/ Region [Ref]	Year	Methodology	Prevalence /100 000	Incidence	Mean age at diagnosis-Male	Mean age at diagnosis in females
Sri Lanka/ Gampaha+Colombo [3]	2010	Hospital based	1.2	0.09	33.4	36.2
Sri Lanka/Gampaha [4]	2011-2012	Community based	NA	0.56	34	

(NA- Not available)

alternative medicine practitioners. The Sri Lankan component of the Asia-Pacific Crohn's and Colitis Epidemiology Study showed the age adjusted incidence rate of CD in Sri Lanka to be 0.56 per 100,000 [4]. In this study, fourteen state and private hospitals with specialist services, in the Gampaha and Colombo districts were used to detect newly diagnosed patients with CD. The patients had to be permanent residents of these districts, over a period of 12 months. The increased incidence reported in this study when compared to the previous study, may have been due to better coverage of the hospitals. However, the findings of these studies may not be generalised, as the two districts that were studied are the most urban districts in Sri Lanka and thus may not reflect the pattern in rural Sri Lanka. Until the date of this review, we could not find other studies specifically aimed at assessing the epidemiology of CD in other South Asian countries.

However, several epidemiological studies have been done among South Asian migrants to the West. A retrospective, community based study by Probert et al [5], showed a minimum incidence of CD of 0.14 per 100,000. In a similar study, Jayanthi et al [6] found the incidence of CD in South Asians to range from 2.4 to 5.4 per 100,000. The highest incidence was among Muslims and the lowest in Hindus.

A study conducted in rural missionary hospitals in some South Asian countries like Bangladesh, India, Nepal, Bhutan and Pakistan found a lower rate of CD compared to UC in India and Bangladesh [7]. One reason for the lower incidence of CD may be due to the diagnostic difficulty in differentiating it from intestinal tuberculosis. An epidemiological study done by Ng et al [8], as a part of Asia-Pacific Crohn's and Colitis Epidemiology study, found the incidence of CD in the studied Asian countries to range from 0.05 to 1.7 per 100,000. The lowest incidence was in Xian, China and highest in Seoul, South Korea. Therefore, the incidence in the South Asian studies was similar to other parts of Asia. The prevalence of CD in South East (SE) Asia ranged from 11.2 to 21 per 100,000 which is considerably

higher than the South Asian region. Although an increase in the incidence and prevalence of CD was documented from SE Asia, the epidemiological trends in South Asia cannot be accurately ascertained due to lack of large scale, population based studies. As expected, the prevalence and incidence of CD in the South Asian region was considerably lower than in Western countries [9].

B. DISEASE CHARACTERISTIC OF CD IN SOUTH ASIA

1. Disease characteristics in Adult CD

The majority of the studies were from India. Other than the more recent studies, most had relatively small sample sizes. There was a male preponderance in most studies. Some of the more recent studies (after year 2000) found the colon to be affected in 21 to 76 % [10 – 15], while other studies found ileocolonic disease to be the commonest [16 – 18]. Extra-intestinal manifestations were seen in 13 to 61.5% of patients in the recent studies. The commonest symptoms were abdominal pain, weight loss and loose stools. A study done by Pai et al [14] found a recurrence rate of 33.3%, whilst Amarapurkar et al [10] found a considerably higher recurrence rate at 78%. Both studies had small sample sizes. (Table 2 [10 – 23]).

2. Complications in adult CD

A few studies from South Asia have documented the complications of CD (Table:3 [10-19, 21, 23]. The commonest complications were: strictures (ranging from 9.5 to 32% of cases) and penetrating disease (in 13-17.5%). Fistulas were also commonly reported. One study found 4.8 % of patients developed a cancer as a complication. Information on other complications such as abscess formation or perforation is limited. A study on the aetiology of sporadic malabsorption syndrome in India, found 9.09% (n=9), were due to CD [24]. However, more recent studies on malabsorption syndromes have shown a lower prevalence of CD, ranging from 2 – 3.2% [25, 26]. Benjamin et al [27] found 52.6% of CD patients to be malnourished.

TABLE 2: DISEASE CHARACTERISTICS (NA- NOT AVAILABLE IN THE PRIMARY MANUSCRIPT. REF – REFERENCE, PAEDIATRIC SERIES INDICATED IN BLUE FONT.)

Author and year [Ref]	Gupta 1962 [19]	Prakash 1976 [20]	Venugopa lan 1980 [21]	Pai 2000 [14]	Khan 2004 [13]	Amara- purkar 2008 [10]	Benja- min 2008 [11]	Das 2009 [12]	Barua 2010 [22]	Suba- singhe 2011 [15]	Pugazh- endhi 2011 [18]	Makh-aria 2012 [17]	Goel 2013 [16]	Sathiya- sekeran 2014 [23]
Region	India, East	India, North	India, South	India, South	Pakistan	India, West	India, North	India, Multi- centre	Bangl- adesh	Sri Lanka, Western	India, South	India, Multi- centre	India, South	India, Multi-centre
Sample size	44	13	21	25	52	26	125	182	41	31	200	409	223	122
Mean age (years)	20-35	NA	30	31.7	40.1	36.6	36	34.5	34	27.4	33	35.9	35	11.0
Male/ female	1:1.4	2.3:1	3.2:1	1.08:1	1:1.2	1.6:1	1.1:1	1.8:1	2.4:1	2.1:1	1.4	1.3:1	1.37	1:1
Follow up (years)	1-5	NA	6-7	0.5-4.5	NA	NA	NA	NA	NA	NA	NA	4	2	NA
Location Ileum/ jejunum	31	0	14.2	0	27	61	12.8	32	NA	9.7	25.5	28.9	25.6	NA
Ileocolon	55	100	43	24	17	NA	37.6	23	NA	12.9	40	39.6	40.4	72.9
Colon	14	0	19	76	21	69	69	41	NA	74.2	26	31.4	21.5	NA
Perianal	0	0	19	20	25	8	20	17	NA	12.9	18.5	6.9	15.2	NA
Upper GI	2.3	0	4.8	0	NA	12	18.4	15	NA	3.2	8.5	NA	12.5	NA
EIM	NA	NA	NA	24	13	61.5	39.2	30	41.4	16.1	NA	56.9	27.4	36.1
Symptoms														
Abdominal pain	16	100	NA	84	83	65	NA	62	NA	77.4	76.5	74.9	69.5	73.8
Loose stools	16	8	4.8	80	88	69	NA	68	NA	51.6	67.5	64.6	57.4	NA
Weight loss	14	38	NA	88	48	69	NA	57	NA	54.8	74.5	66.1	71.3	NA
Abdominal lump	31	69	24	24	15	8	NA	6	NA	NA	NA	4.4	NA	NA
Intestinal obstruction	20	15	14.3	16	NA	19	NA	28	NA	NA	NA	NA	NA	NA
Acute abdomen	14	NA	23	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Fever	NA	46	NA	16	37	23	NA	30	NA	19.4	49	42.9	23.3	39.3
GI bleeding	NA	NA	NA	44	52	31	NA	67	NA	12.9	46	42.2	35.4	NA

There was a significant difference in the percentage of those malnourished in the active and remission phases of the disease (82.8% vs. 38.9%). This was despite there being no difference in the dietary intake between the two phases.

A case control study from Sri Lanka found 10.7% of CD patients to have osteoporosis by peripheral dual energy X-ray absorptiometry scanning and this was significantly lower than in UC patients [28]. In a similar case control study from India, two thirds of CD patients had low bone mineral density particularly at the hip and spine [29]. The calcium intake in CD patients was inadequate in the Indian study. In a case control study of 34 CD patients and controls done in India, 25 (OH) Vitamin levels were significantly lower in the CD patients, and had a significant negative correlation with disease severity and significant positive correlation with exposure to sunlight [30]. These findings points towards multifactorial impacts on the calcium and bone metabolism in CD patients.

3. Disease characteristics and complications in Paediatric CD

The first report on paediatric CD in South Asia was from Chennai. The authors described ten children (between the ages of 5-15 years), eight of whom primarily had colonic disease. Complications (such as stricture and fistula) were noted in four, rectal bleeding was seen in 25% and extra intestinal manifestations in 25%. Except for one patient, all others were managed medically [31].

A multicentre study from India, found the majority of paediatric patients to present with abdominal pain (73.8 %) and fever (39.3 %). Ileocolonic CD was the commonest (72.9 %) manifestation and extra-intestinal manifestations were seen in 36.1 %. A high degree of complications such as anaemia (64.7 %) and growth failure (76.2 %) were also seen. In addition, 27% had fistulae, perianal abscesses, strictures or a perforation and Biological agents were used in 12.2% [23].

In South Asia, a male preponderance was noted, similar to other parts of Asia and different from the West (where an equal sex distribution was seen) [32]. In other Asian countries, ileo-colonic disease predominates, whilst in the West, colonic, ileal and ileocolonic disease occurs in equal proportions [32]. In contrast, in South Asia, some series report a predominance of isolated colonic disease [10 – 15], whilst a few found ileo-colonic disease to be commonest [16 – 18]. Comparing the disease characteristics and complications with other Asian and Western countries has been difficult, as the studies have not used a standardized classification system [32]. In general, studies from the West

have shown inflammatory, stricturing, penetrating and perianal CD rates of 62–81%, 5–27%, 8–14% and 11–27% respectively. Whereas studies from Asia (which are mostly hospital based), have found inflammatory disease in 40–69%, stricturing disease in 20–28%, and penetrating disease in 10–31% of CD patients [32]. In studies from South Asia, stricturing was noted in 9.5-32% and penetrating disease in 13 – 17.5%.

C. AETIOPATHOLOGY AND RISK FACTORS OF CROHN'S DISEASE

A case control study done by Pugazhendhi et al [18] analysed the environmental associations of CD in a cohort of patients from South India. Positive associations were noted with urban residence, safe drinking water and the availability of piped water in the house both in childhood and at the current age. Protective associations were noted with a history of regular fish consumption and presence of cattle in the house compound currently. No association was established with smoking or history of appendectomy [18]. It is postulated that improvement in sanitation, hygiene, prosperity and change in lifestyle may significantly increase the risk of CD, and may be responsible for the recent increase in the reports of this disease from South Asia [2, 33].

D. QUALITY OF LIFE OF CROHN'S DISEASE PATIENTS IN SOUTH ASIA

Although there are several reports on the disease characteristics, studies on the quality of life among CD patients remains a poorly studied area.

E. GENETICS OF CD IN SOUTH ASIA

Only a few studies have aimed to analyse the genetic associations of CD in South Asia and all studies were from India (Table 4 [34 – 38]). Nucleotide oligomerization domain (NOD)-2 variants associated with CD patients in the West, has not been described in South Asian populations. This is similar to observations in some other Asian populations such as Chinese, Japanese, Korean, and Malaysian populations. A study by Pugazhendhi et al [37] found NOD2 mutations commonly found in patients from the West to be uncommon in their patients. Pugazhendhi et al [34], using a case control study, sequenced the NOD2 gene, and looked for novel associations. Eight polymorphisms were noted (rs2067085, rs2066842, rs2066843, rs1861759, rs2111235, rs5743266, rs2076753, and rs5743291), the latter four described for the first time in Indians. None of these polymorphisms were associated with CD.

Mahurkar et al [35], using a case control study format, studied variants in the NOD2 and interleukin-23 receptor (IL23R) gene in Indian IBD patients. Three of the NOD2 disease-susceptible variants, R702W, G908R, and 1007fs in NOD2 were monomorphic in these patients. Three other single nucleotide polymorphisms (P268S, R459R, and R587R) had a comparable minor allele frequency among patients and controls. This study suggested that variants in the NOD2 gene and the protective variant R381Q in the IL23R gene was not associated with IBD.

A case control study assessed TNF alpha gene polymorphisms in CD. The TNF-A -863 AA genotype was associated with enhanced susceptibility for CD and C/A/C haplotypes was associated with an increased risk. Variant genotypes of IL-4 (B1/B2 + B2/B2) were absent in colonic type CD. Furthermore, IL-10 polymorphisms did not demonstrate any association with CD. None of the polymorphisms were associated with steroid treatment or surgery [36].

Another case control study analysed IL-1Ra gene polymorphisms. The frequency of allele 2 in CD was higher than that in UC and healthy controls. Alleles 3 and 4 were absent in patients with CD, whilst allele 5 was absent in all three groups. Ethnic differences, genetic heterogeneity and sample size could account for the observed differences from studies done in the West.

Despite the limited studies done in South Asia, novel findings related to genetic association were noted. Novel associations in relation to TNA-alpha (C-863A) and IL-1Ra genes were noted in Indians. New NOD2 mutations were noted CD in Indians (p268S), similar to Malaysians (JW1 mutation) and Han Chinese. Global variations in the genetic mutations were noted in the West and other Asian countries [32]. Therefore, further studies are required to look for associations in relation common genetic mutations described in other parts of the world such as the autophagy-related protein16-liked 1(ATG16L1) mutation, Interleukin (IL)-23R mutation, Gly149Arg and other tumour necrosis factor (TNF) polymorphisms. The novel genetic mutations noted in this population of rising incidence may be helpful in discovering new knowledge for understanding the pathogenesis of the disease.

F. CROHN'S DISEASE VS INTESTINAL TUBERCULOSIS

The relatively low prevalence of CD in South Asia may be because of the diagnostic dilemma of a high prevalence of TB. In one report, nearly a quarter of patients with CD were being treated as intestinal tuberculosis [39]. This is because abdominal TB and CD may be difficult to

differentiate both clinically and radiologically. However, the distinction between the two is essential for the management and exclusion of TB is mandatory before starting treatment for CD [40]. Studies have shown that histological analysis by segmental colonoscopic biopsies is often useful in the differentiation of TB from CD [41]. Another study from India has shown that anti-Saccharomyces cerevisiae antibody (ASCA) was not useful in differentiating between CD and intestinal TB [42].

Pulimood et al [43], have suggested that certain features such as fever, pulmonary involvement, abdominal distension, peritoneal nodules and ascites were in favour of TB, while features such as recurrent intestinal obstruction, diffuse small bowel involvement, multiple strictures, internal fistulas, deep linear ulcers and cobblestone appearance were more in favour of CD. In a recent study, using a multivariate analysis, Makharia et al [44], have analysed clinical, endoscopic and histological parameters as predictors in the differentiation of CD and intestinal TB. Features such as blood in the stool, weight loss, focally-enhanced colitis, and involvement of the sigmoid colon were the most essential features for differentiation between intestinal TB and CD. Thus a combination of a good clinical history with colonoscopy, biopsies, cultures, and radiology would be necessary to make a diagnosis in the majority of cases.

G. TREATMENT OF CD IN SOUTH ASIA

In South Asia, studies on treatment of CD were mostly descriptive in nature. No case control or randomised control studies have been done to compare outcomes in South Asian patients. The common pharmacological agents used for remission induction and maintenance are 5-Amino salicylic acid (5-ASA), prednisolone and azathioprine (Table 5 [12, 15, 16, 39]). Up to date, there have been no prospective studies on efficacy, tolerance and the side effects of these therapies in South Asian CD patients.

Surgery was the treatment modality in a considerable proportion of patients. The common indications for surgery are: strictures, perforations, fistulae and perianal disease. The commonest surgical modality used was resection with anastomosis and other modalities included strictureplasty, resection with exteriorisation and fistula repair [12, 15, 16, 39].

TABLE 3: COMPLICATIONS (NA- NOT AVAILABLE IN THE PRIMARY MANUSCRIPT)

Author and year [Ref]	Gupta 1962 [19]	Venugopalan 1980 [21]	Pai 2000 [14]	Khan 2004 [13]	Amara-purkar 2008 [10]	Benjamin 2008 [11]	Das 2009 [12]	Suba-singhe 2011 [15]	Pugazhe-ndhi 2011 [18]	Makh-aria 2012 [17]	Goel 2013 [16]	Sathiya-sekeran 2014 [23]
Region	India, East	India, South	India, South	Pakistan	India, West	India, North	India, Multi-centre	Sri Lanka, Western	India, South	India, Multi-centre	India, South	India, Multi-centre
Sample size	44	21	25	52	26	125	182	31	200	409	223	122
Complications	NA	NA	NA	NA	NA	NA	NA	NA	23.5 – stricturing 17.5- penetrating	NA	29.1- stricturing 13- penetrating	27
Fistula	4.5	24	NA	14	12	11.2	8	NA	NA	4.4	NA	NA
Stricture	32	9.5	16	15	NA	29.6	28	19.4	NA	18.8	NA	NA
Abscess	NA	4.8	4	NA	NA	NA	2	NA	NA	NA	NA	NA
Perforation	NA	4.8	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cancer	NA	4.8	0	NA	0	0	0	NA	NA	NA	NA	NA
Surgical treatment	100	100	NA	NA	35	NA	37	41.9	31	15.2	32.7	NA
Recurrence	11.4	33.3	NA	NA	78	NA	NA	NA	NA	NA	40	NA
Family History	NA	NA	NA	NA	NA	NA	NA	NA	NA	4.6	0.9	NA

TABLE 4: GENETICS ASSOCIATIONS OF CD IN SOUTH ASIA

Country-Place [Ref]	N	Year	Methodology	Genes studied	Positive association with CD	Other findings
India-South [34]	310	2013	Case control	NOD2 gene, rs2067085, rs2066842, rs2066843, rs1861759, rs2111235, rs5743266, rs2076753, and rs5743291	None	The SNPs rs2066842 and rs2066843 were in significant linkage disequilibrium.
India-South [35]	241	2011	Case control	Variants in NOD2 and interleukin-23 receptor (IL23R)	None	Monomorphic status for three common disease-susceptible variants, R702W, G908R, and 1007fs in NOD2; three other single nucleotide polymorphisms, P268S, R459R, and R587R, had a comparable minor allele frequency in patients and controls
India-North [36]	153 (IBD)	2011	Case control	TNA-alpha (C-863A)	Associated with enhanced IBD susceptibility more so for UC than CD	Variant genotypes of IL-4 (B1/B2+B2/B2) were absent in colonic type CD. No association with steroid treatment or surgery.
India-South [37]	82	2008	Case control	The 3 common NOD2 mutations	None	The described mutations were uncommon CD patients
India [38]	21	2004	Case control	IL-1Ra polymorphism	Frequency of allele 2 in CD was higher than that in UC and healthy controls. Alleles 3 and 4 were absent in patients with CD	Allele 5 was absent in both cases and controls.

TABLE 5: SUMMARY OF TREATMENT OF CD IN SOUTH ASIA (NA – NOT AVAILABLE)

Author [Ref]	Prakash [39]	Goel [16]	Das [12]	Subasinghe [15]
Year	2008	2013	2008	2011
Place	India, South	India	India	Sri Lanka
Total No	23	223	182	31
No underwent Surgery	23, 100%	73, 32.7%	66, 36.3%	13, 41.9%
Multiple Surgeries	9, 39.1%	10	NA	0
Postop morbidity	9, 39.1% (Anastomotic leakage-6)	10	NA	NA
Postop mortality	1, 4.34%	NA	NA	NA
Pharmacological agents used	5-ASA, prednisolone, azathioprine, 6-mercaptopurine	5-ASA, prednisolone, azathioprine	5-ASA, steroids, azathioprine, methotrexate, salazopyrine	5-ASA, Azathioprine, prednisolone, sulphasalazine
Indication	NA	NA	NA	NA
Stricture	23, 100%	NA	NA	7, 53.8%
Perforation	5, 21.7%	NA	NA	NA
Fistula	8, 34.8%	NA	NA	5, 38.4%
Perineal disease	NA	22, 30.1%	NA	1, 7.7%

A study by Prakash et al [39], described the postoperative complications of CD patients. Nine patients (30%) developed postoperative complications, with 21% (n=6) anastomotic leaks. Factors associated with anastomotic leakage were: preoperative anaemia, malabsorption, growth retardation, immunosuppressant therapy and mid-small bowel resection. The indication for surgery, type or extent of disease and creation of a diverting stoma did not affect the postoperative outcome.

Goel et al [16], analysed the predictive factors for surgery in CD. Significant predictors of surgery were: male sex, small bowel disease and perianal disease. Total duration of illness did not independently predict the need for surgery. One case report was published on the use of biologic agents [45] and another descriptive study on paediatric CD mentioned that 12.2% were treated with biologic agents [23]. The use of biologics in CD in South Asia is an area that needs further research.

A retrospective study among the Indian population by Davavala et al [46], analysed mutations in the Thiopurine methyltransferase (TPMT) enzyme (which plays a key role in the metabolism of azathioprine/6-mercaptopurine) gene. They found the *TPMT* genotype to be wild type in 95.23 % and heterozygous in 4.77 %, with no patient having a homozygous mutation. Of the participants, 6.8 % of who received azathioprine developed neutropenia; blood counts normalized on cessation of the drug in all. Furthermore, neutropenia was equally common in patients with and without the *TPMT* gene mutation.

A study conducted in South Asia by Pugazhendhi et al [18], did not find an association with appendectomy and CD, which is comparable to findings from the West. An association with smoking was not established, similar to some other Asian countries and in contrast to some Western populations [32]. In a South Asian study, positive associations were noted with urban residence, safe drinking water and availability of piped water in the house which may reflect on the improved sanitation and hygiene [18]. Although a few studies postulate an association with hygiene and socio-economic development, large population based studies are needed to confirm this [2].

The preferred pharmacological agents in South Asia such as 5- Aminosalicylate and azathioprine were also used commonly in other parts of Asia. The level of usage varied between countries. Although biologic agents were frequently used for CD in some developed Asian countries (at levels similar to the West), reports on the use of biologic agents for CD in South Asia is scarce.

The cumulative rate of surgery in the series of studies from South Asia was 15.2 – 41.9%. The cumulative surgery rates of other Asian countries varied greatly. Most studies originated from Hong Kong, China, Korea and Japan and their cumulative rates were 29% at 10 years, 58.3% at 10 years, 32.8% at 10-15 years and 46.3 – 80.1% at 10 years, respectively. These values were comparable to data from Western countries. The relatively lower rates of surgery in the South Asian CD series may be due to the lower duration of follow up. It is still not clear whether the variation in surgical rates in Asia and the West are due to differences in

clinical practice or disease severity. Goel et al [16], found male sex, small bowel disease and perianal disease to be significant predictors of surgery. Multivariate analyses from China found stricturing and penetrating disease and smoking habit to be independently associated with increased risk of surgery, whereas in Japan female gender and ileal disease were independent risk factors for surgery [32].

III. CONCLUSION

We have reviewed the available data on CD in South Asia. The studies of CD from South Asia are mainly from parts of India and the Western province of Sri Lanka. There are no randomized or case control studies on treatment modalities of CD in South Asia and most studies so far are descriptive. Studies on the efficacy and safety of novel pharmacological agents/biologics are limited. Furthermore, as the findings so far, cannot be generalized to the South Asian region (as there is much ethnic and cultural diversity within each country and between countries in South Asia), it is important that more well designed collaborative studies be done within this region. More population based studies of CD in South Asia are needed to understand current disease burden and epidemiological trends. Properly designed clinical studies are needed to better characterize the disease patterns, treatment modalities and long term outcomes of CD in South Asia.

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