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Comparison between Demographic profile and Clinical presentation of Gastrointestinal Tuberculosis and Crohn's Disease Patients in a Tertiary Care Hospital

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Abstract:
Background: *Distinguishing Crohn's disease (CD) from gastrointestinal tuberculosis (GITB) is clinically challenging but important for patient management. Objectives: The purpose of the present study was to compare the demographic profile and clinical presentation of gastro- intestinal tuberculosis (GITB) and Crohn's disease (CD) patients.* ***Methods:*** *This observational cross-sectional study was carried out in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, Dhaka from February 2014 to July 2015. Thirty-five patients diagnosed as GITB and 35 patients diagnosed as Crohn's disease according to diagnostic criteria were included in the study. A predesigned questionnaire was used for collecting data. All information including demographic profile, history and clinical features, laboratory investigations, colonoscopy findings and biopsy findings were recorded.* ***Results:*** *Out of 35 patients of GITB 24 patients were male and out of 35 patients of CD 22 patients were male. So male was more than female in both groups. Most of the GITB patients were illiterate or less educated but most of the CD patients were educated up to secondary level or above. Abdominal distension was higher in GITB patients (85.7%) than that of CD patients (11.4%) and the differences were statistically significant. Vomiting (40%), bloody diarrhea (28.6%) and features of sub-acute intestinal obstruction (45.7%) were more common in CD than those of GITB patients ($p<0.05$). Anaemia was more common in CD patients than GITB patients but the differences were not statistically significant. Clubbing, angular stomatitis, smooth tongue, leukonychia, edema, fistula in Ano and extra intestinal manifestations (arthritis, oral ulcer, episcleritis) were more common in CD than that of GITB patients and the differences were statistically significant.*
Conclusion: *A combined evaluation of demographic profile, clinical features, endoscopic features and histological reports is the key to differentiate between GITB and CD.*
Keywords: *Distinguishing Crohn's disease (CD), Gastrointestinal tuberculosis (GITB), Endoscopic features.*

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I. Introduction

In Western countries, the incidence of inflammatory bowel disease (IBD) has progressively increased since 1935. [1] Crohn's disease (CD) has been increasing worldwide; it is generally believed to be rare in developing countries like Bangladesh. Indian migrants in Western countries have shown increased incidence of

IBD, more so in the second generation of immigrants. In India, the incidence of CD increased progressively in the last decade. [2] Tuberculosis (TB) remains widely prevalent in developing countries such as Bangladesh. Also, it is being increasingly encountered in industrialized nations due to pandemic of human immunodeficiency virus infection and trans-global migration. [3] There is a close resemblance in clinical, radiological, endoscopic, surgical and histological features of CD and gastrointestinal tuberculosis (GITB), thus differentiation of these two conditions remains a major challenge to clinicians. [4]

There are many factors that lead to misdiagnosis. Both the diseases have marked overlap in demographic, clinical, radiological, endoscopic and surgical findings. They can involve any part of gastrointestinal tract. Both are granulomatous diseases, so inability to find caseating granuloma on histology can lead to erroneous or no confident diagnosis by a pathologist. Routine tests for diagnosis of TB such as AFB smear examination, using conventional Ziehl- Neelsen stain, traditional AFB culture using egg-based or agar-based media or Guinea pig inoculation, lack sensitivity and/or are time-consuming. Smear examination using fluorescence technique and culture with Bactec technique are more rapid and more sensitive. As GITB is a paucibacillary disease, sensitivity for detecting mycobacterium in clinical specimens by any of the above methods remains poor. Although many serological tests for TB are commercially available, they are far from satisfactory in diagnostic dilemma. [5]

Endoscopic features or surgical finding of deep linear/serpiginous ulcers/fissures and cobble-stone appearance are more common in CD. None of the clinical or morphological features are exclusive for either of the diagnoses. Recently, Pulimood have reported that on mucosal biopsy, in addition to AFB detection, large granuloma, cascation, band of epitheloid histiocytes in ulcer base favour of diagnosis of TB; whereas non-caseating granuloma, focal crypt-related inflammation and transmural inflammation are in favour of diagnosis of CD. [6]

Serological test for IBD is being investigated as diagnostic markers for IBD. Sensitivity of positive ASCA for diagnosis of CD reaches up to 76%. [2] These data come from countries where tuberculosis is uncommon and control population in these studies did not include patients with GITB. In the different study, it was found that (1) serological markers were not significantly different between CD and GITB; and (2) prevalence of positive ASCA was much lower in patients with CD than the reported incidence from Westernm countries. A recent study by another center in India showed that ASCA was not helpful in differentiating CD from GITB. [7] TB PCR is found to be highly specific for GITB, but had poor sensitivity.

II. Methodology

This cross-sectional study was carried out in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU) during February 2014 to July 2015 for a period of eighteen months. A total 70. patients, among them 35 patients diagnosed as GITB and 35 patients diagnosed as CD were enrolled in this study. Patients diagnosed as either GITB or CD age 18 years or more of both sexes were selected as study population. **Data Collection and Processing:** After taking consent and matching eligibility criteria, data were collected from patients on variables of interest using the predesigned structured questionnaire by interview, observation. To collect data, face to face interview has been carried out with a standardized semi-structured questionnaire. Alongside, the medical records of the patients have been reviewed. Data regarding sociodemographic background, diabetic and smoking status has been collected and recorded. Collected data were edited and Statistical analyses of the results were be obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24). Frequency and percentages have been depicted for qualitative data and mean and standard deviation has been calculated for quantitative data.

III. Result

This observational cross-sectional study was conducted in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. This study was conducted a total 70 patients, among them 35 patients diagnosed as GITB and 35 patients diagnosed as CD were enrolled in this study. Patients diagnosed as either GITB or CD age 18 years or more of both sexes were selected as study population.

Table I: Distribution of patients according to age in two groups (n= 35+35)

Age (years)	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
18-20	5(14.3)	1 (2.9)	0.088
21-30	18 (51.4)	13 (37.1)	0.229
31-40	6 (17.1)	12 (34.3)	0.101
41-50	2 (5.7)	4(11.4)	0.393
>50	4 (11.4)	5(14.3)	0.721
Total	35 (100.0)	35 (100.0)	0.181

Mean ± SD	30.31±11.96	35.54±11.86	0.071

t test was done to measure the level of significance.

Table I shows age distribution of the patients. Mean age of GITB and Crohn's disease was 30.31 ± 11.96 years and 35.54 ± 11.86 years respectively.

Table II: Distribution of patients according to gender in two groups (n=35+35)

Sex	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Male	24 (68.6)	22 (62.9)	0.615
Female	11 (31.4)	13 (37.1)	
Total	35(100)	35(100)	

Chi-square test was done to measure the level of significance.

Table II shows male were predominant than female in both groups.

Table III: Distribution of patients according to clinical examination in two groups (n=35+35)

Clinical examination	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Anaemia	23 (65.7)	30 (85.7)	0.051
Clubbing	0 (0.0)	20 (57.1)	<0.001
Angular stomatitis	5(14.3	18 (51.4)	0.001
Smooth tongue	4 (11.4)	14 (40.0)	0.006
Koilonychia	1 (2.9)	5(14.3)	0.088
Leukonychia	1 (2.9)	10 (28.6)	0.003
Edema	0 (0.0)	8(22.9)	0.003
Ascites	7 (20.0)	0 (0.0)	0.005
Abdomina lymphadenopathy	12 (34.3)	1(2.9)	0.001
Abdominal lump	6 (17.1)	8 (22.9)	0.550
Fistula in Ano	0 (0.0)	8 (22.9)	0.003
Extraintestinal manifestation (arthritis oral ulcer, episcleritis)	0 (0.0)	21 (60.0)	<0.001
BMI (Mean ± SD) kg/M²	17.98±3.74	19.05±3.07	0.199

Chi-square test was done to measure the level of significance.

Table III shows clinical examinations of both groups. Incidence of ancamia, clubbing, malnutrition, angular stomatitis, smooth tongue, leukonychia, edema, fistula in Ano and extra intestinal manifestation were significantly higher in Crohn's disease than that of GITB. Mean BMI was lower in GITB than Crohn's disease patients. Incidence of Ascites and Abdominal lymphadenopathy were higher in GITB than that of Crohn's disease patients the difference was statistically significant in each.

Table IV: Distribution of patients according to history of past illness in two groups (n=35+35)

History of past illness	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Previous history of TB	1 (2.9)	2(5.7)	0.555
Blood transfusion	4 (11.4)	17 (48.6)	0.001
Surgery (laparotomy) [Resection & anastomosis of intestine) (during diagnosis)	2 (5.7)	15 (42.8)	0.001
Drug history (Anti-TB drugs) [before diagnosis)	1 (2.9)	2 (5.7)	0.555
Family history			
Contact with TB	12 (34.3)	0 (0.0)	<0.001
Crohn's disease	0 (0.0)	2(5.7)	0.151

Chi-square test was done to measure the level of significance.

Table IV shows the history of past illness in both groups. History of blood transfusion and laparotomy were significantly higher in Crohn's disease comparing to GITB. Table also shows history of similar disease in both groups. Contact with TB was found in 12 (34.3%) GITB patients and 1 (0.1%) in CD patients. Different was statistically significant.5.7% of CD Patients had family history of Crohn's disease but none in GITB patients.

Table V: Distribution of patients according to laboratory findings in two groups (n=35+35)

Laboratory findings	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Hb (gm/dl)	10.32±2.15	9.48±1.20	0.047
ESR (mm in 1" hr)	75.68±28.85	45.62±19.77	<0.001
TC of WBC (per cumm)	8.22±3.04	8.91±2.13	0.274
TPC (per cumm)	2.72±0.60	3.53±1.30	0.006
CRP (gm/dl)	23.06 ±20.85	44.39±25.04	<0.001
Albumin (g/l)	35.37±5.13	29.46 ±5.98	<0.001
PBF			**<0.001**
Microcytic hypochronic anemia	10 (28.6)	9.(25.7)	
Normocytic normochromic anemia	1 (2.9)	12 (34.3)	
Combined deficiency anemia	0(0.0)	9(25.7)	
MT (Positive)	15(42.9)	2(5.7)	0.001
CXR P/A view (Pulmonary involvement)	8(22.9)	0(0.0)	0.003

Independent t-test was done to measure the level of significance.

Table V shows laboratory findings of the patients of both groups. Mean Hb, ESR and albumin were more in GITB patients than that of Crohn's disease patients. The differences were statistically significant. But mean value of TC of WBC, TPC and CRP were more in Crohn's disease patients than that of GITB patients. The differences were statistically significant. Regarding PBF, incidence of microcytic hypochronic anemia was higher in GITB than Crohn's disease but incidence of normocytic normochronic anemia and combined deficiency anemia were higher in Crohn's disease than GITB and the difference was statistically significant. Incidence of MT (+ve) and CXR P/A view (abnormal) were higher in GITB than Crohn's disease and the differences between two groups were statistically significant.

Table VI: Distribution of patients according to Barium follow through in two groups (n=35+35)

Barium follows through	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Features			
Stricture& Dilatation	6 (17.1)	16 (45.7)	0.010
Strings sign	0 (0.0)	1(2.9)	0.314
Ulcer spike	2 (5.7)	0 (0.0)	0.151
Site			
Only ileum	6 (17.1)	8 (22.9)	0.550
Only jejunum	0 (0.0)	3 (8.6)	0.077
Multiple site	0 (0.0)	5 (14.3)	0.020

Chi-square test was done to measure the level of significance.

Table VII shows barium follow through of the patient in both groups. Stricture & dilatation was significantly higher in Crohn's disease. Incidence of multiple site involvement was significantly higher in Crohn 's disease.

Table VII: Distribution of patients according to colonoscopy findings in two groups (n=35+35)

Colonoscopy findings	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Skip lesions	2 (5.7)	15 (42.9)	<0.001
Deep linear/ longitudinal ulcers	2 (5.7)	10 (28.6)	0.011
Scattered ulcer	7 (20.0)	15 (42.9)	0.039
Deep transverse ulcers	13 (37.1)	0 (0.0)	<0.001
Aphthous ulcers	1 (2.9)	7 (20.0)	0.024
Cobble stone appearance	1 (2.9)	9 (25.7)	0.006
Pseudo polyps	0 (0.0)	8(22.9)	0.003
Nodular lesion	10 (28.6)	3 (8.6)	0.031
Luminal narrowing	3 (8.6)	4 (11.4)	0.690
Histopathology findings			
Granuloma	19 (54.3)	5 (14.3)	<0.001
a) Caseating	15 (42.9)	0 (0.0)	<0.001
b) Non-caseating	4 (11.4)	5(14.3)	0.721

Transmural inflammation	0 (0.0)	16 (42.8)	0.001
Interpreted nonspecific chronic inflammation	0 (0.0)	8 (22.9)	0.003
AFB smear positivity	4 (11.42)	0 (0.0)	0.039
TB PCR positively	8 (22.85)	0 (0.0)	0.003

Chi-square test was done to measure the level of significance

Table VII shows colonoscopy findings of the patients of two groups. Incidence of skip lesions, deep linear/ longitudinal ulcers, aphthous ulcer, cobble stone appearance and pseudo polyps were significantly higher in Crohn's disease than GITB. But the incidence of deep transverse ulcers and nodular lesion were significantly higher in GITB than Crohn's disease. Table also shows incidence of caseating granuloma, AFB smear positivity and TB PCR positivity were significantly more common in GITB than Crohn's disease. But incidence of transmural inflammation was more common in Crohn's disease than GITB.

Table X: Distribution of patients according to site of involvement in groups (n=35+35)

Site of involvement	Group-A (GITB) n(%)	Group-B (Crohn's disease) n(%)	P value
Both small & large intestine	15 (42.9)	16 (45.7)	0.810
Only small intestine	10 (28.6)	10 (28.6)	0.322
Jejunum	1 (2.9)	2 (5.7)	0.555
Ileum	10 (28.6)	14 (40.0)	0.314
Only large intestine	5 (14.3)	9(25.7)	0.771
Cecum	7 (20.0)	8 (22.9)	0.771
Ascending colon	2 (5.7)	4 (11.4)	0.393
Transverse colon	1 (2.9)	2 (5.7)	0.555
Descending colon	1 (2.9)	3 (8.6)	0.303
Sigmoid colon	0 (0.0)	3 (8.6)	0.077
Other sites	5 (14.3)	0 (0.0)	0.020
Abdominal lymph node	2 (5.7)	0 (0.0)	
Peritoneum	3 (8.57)	0 (0.0)	

Chi-square test was done to measure the level of significance.

Table X shows site of involvement in two groups. Incidence of site of involvement was near similar in CD and GITB group and statistically not significant. But abdominal lymph node and peritoneum involvement were found only in GITB.

IV. Discussion

Differentiation between Crohn's disease and intestinal tuberculosis is a diagnostic challenge as they present with similar clinical, radiological, endoscopic and histological features. A definitive diagnosis in these cases is extremely important before initiation of treatment to avoid the toxicity of unnecessary anti-tuberculous therapy in patients with Crohn's disease and potentially fatal immunosuppressive treatment in patients with intestinal TB. There are multiple study reports to differentiate between two conditions in developing and developed countries. But there is no such study in Bangladesh. Thirty-five patients diagnosed as GITB and 35 patients diagnosed as Crohn's disease age 18 years and above were included in this study.

Regarding age, mean age of GITB patients were 30.31± 11.96 years and Crohn's disease patients were 35.54 ± 11.86 years respectively. There was no significant difference in age between these two groups. Most of the incidence of GITB was in age group of 21-30 years but Crohn's disease was seen among the age group of 31-40 years. Mean age was higher in CD group than GITB group Makharia (2010) and Larsson (2014) which are similar with our study report. [8,9] Barua studied on 41 Bangladeshi Crohn's disease patients in 2010 and found that mean age was 34±11.8 years and peak age group was 21- 30 years, which is also consistent with our study report. [10]

Regarding gender, male was more common than female in both groups. In GITB group, male was 68.6% and female was 31.4%. In crohns' group, male was 62.9% and female was 37.1%. There was no statistically significant difference between these two groups. In 2010, Barua studied on 41 crohns' disease patients, among them 70.7% were male and 29.3% were female with male to female ratio was 2.4:1 which is consistent with our study report. [10]

Reporting eshrcational level, UITD was more common among therate people but Crohn's disease was more common among educated propter and the differences were statistically significant. Crohn's disease patients were more chicated than GITI patients which are consistent with cur study report. [9] Regarding presenting

complain, fever (100.0%), anorexia (97.1%) and weight Joss (94.3%) were common in GITB patients whereas they were 48.6%, 65.7% and 88.6% respectively in Crohn's disease patients. Differences were statistically significant. Similar to this study prevalence of fever and weight loss was more in GITB than CD. [8, 2, 11] Abdominal distension was significantly higher in GITB patients (85.7%) than that of Crohn's disease patients (11.4), this result is consistent with results of Pulimood study. [12] Vomiting (40.0%) vs (17.1%), bloody diarrhoea (28.6%) vs (5.7%) and sub-acute intestinal obstruction (45.7%) vs (11.4%) were more common in CD than that of GITB patients. The differences were statistically significant. Our study report is consistent with the study report of Patel and Dutta. [2, 13] They reported that blood mixed stool was seen more often in patients with CD than GITB.

In this study, mean duration of illness before diagnosis in GITB group was 1.35 1.66 years and CD group was 6.71 4.01 years. The difference was statistically significant. Duration of illness was higher in CD than GITB in our study which is consistent study report of Makharia, Patel and Dutta. [2, 8, 13] They reported that the median duration of the disease was significantly longer in patients with CD (53.3±62.8 months) than in patients with intestinal tuberculosis (23.4±39.7 months). Regarding physical findings, BMI was lower in GITB (17.98±3.74) than that of Crohn's disease (19.05 ± 3.07) patients and the difference was not statistically significant. Larsson in 2014 reported similar findings which is consistent with our result. [9] Regarding physical findings, anemia was 65.7% in GITB group and 85.7% patients in CD group. The difference was statistically significant. Anaemia was significantly higher in CD than GITB which is consistent with our study report. [14]

Clubbing (57.1%) vs (0.0%), malnutrition (51.4%) vs (2.9%), angular stomatitis (51.4%) vs (14.3%), smooth tongue (40.0%) vs (11.4%), leukonychia (28.6%) vs (2.9%), edema (22.9%) vs (0.0%), fistula in ano (22.9%) vs (0.0%) and extra intestinal manifestation (60.0%) vs (0.0%) were more common in CD than that of OITD patients and the differences were statistically significant in esch Fistula in ano was higher in CD then GITD which was consitent with our study. [12] Laboratory finding of the patient were recorded. Mean Hb (10.32± 2.15 vs 9.48 & 1.20) in gm/dl, ESR (75.68 ±28.85 vs 45.62± 19.77) mm in 1 hour and albumin (35.37±5.13 vs 29.46 & 5.98) in gm/l which were in higher value in GITB patients than that of Crohn's disease patients. The differences were statistically significant. In 2011 Dutta reported that ESR was significantly higher in GITB than CD and Hb and Albumin were less in CD than GITB patients which are consistent with our result. [13] But mean value of TC of WBC (8.91±2.13 vs 8.22 & 3.04) in per cumm, TPC (3.53 1.30 vs 2.72 0.60) in per cumm and CRP (44.39 ±25.04 vs 23.06 ± 20.85) in gm/dl were higher in CD than that of GITB patients. The differences were statistically significant. CRP was higher in CD than GITB, which is consistent with our result. [14]

Regarding PBF, incidence of microcytic hypochronic anemia was higher in GITB than Crohn's disease but incidence of normocytic normochronic anemia and combined deficiency anemia were higher in CD than that of GITB patients and the difference was statistically significant. Incidence of MT positivity and pulmonary involvement were higher in GIT than Crohn's disease patients and the differences between two groups were statistically significant. In Pulimood study, pulmonary involvement was (34.5% vs 8.2%) significantly higher in GITB than Crohn's disease patients, which has similarity with our study result. [12] Regarding barium follow through repot, stricture & dilatation in the small intestine was significantly higher in Crohn's disease patients. Incidence of multiple site involvement was significantly higher in Crohn's disease which similar to the study reported by Dutta in 2011. [13]

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

V. Conclusion

In conclusion, differentiating CD from GITB continues to be a challenging problem. There are some features which are common in both diseases but some features are exclusively present in either of two conditions. So combined evaluation of clinical features, endoscopic features, radiological reports, histological reports and sometimes response to treatment is the key to differentiate between two conditions. We need to continue to develop new tests to help clinicians for differentiating between the two conditions.

VI. Recommendation

This study can serve as a pilot to much larger research involving multiple centers that can provide a nationwide picture, validate regression models proposed in this study for future use and emphasize points to ensure better management and adherence.

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