Colonoscopic Findings and Histological Changes in Patients Suffering from Ankylosing Spondylitis with Normal Bowel Habit

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Abstract
Ankylosing Spondylitis is a form of spondyloarthropathies characterized by chronic inflammation of the joints of axial skeleton, manifested clinically by pain and progressive stiffening of spine. It is evidenced that sero-negative spondyloarthropathies are closely related with gut inflammatory lesions. This inflammatory gut lesions may be clinically silent or with abnormal bowel symptoms. This observational study was done with an intension to see the inflammatory gut lesions in ankylosing spondylitis patients having normal bowel habit. In this study thirty eight ankylosing spondylitis patients were selected by New York revised criteria having normal bowel habit. All patients were subjected to full colonoscopy with biopsy. Only 7.89% patient showed macroscopic abnormalities (Grade-1 & 2) and 15.87% had microscopic non-granulomatous inflammatory lesion of grade 1 & 2 on biopsy. This study concluded that gut inflammatory lesions in ankylosing spondylitis patients with normal bowel habit is not remarkable. So before making concrete opinion, further large sized comparable study with & without bowel symptoms can be warranted.

Introduction
Ankylosing Spondylitis (AS) is the prototype of group of disorder called spondyloarthropathy characterized by primarily axial joint involvement often with peripheral arthropathy and enthesopathy. Association between infective gut lesion attributed by salmonella, shigella, yersinia and reactive arthritis is clearly established. Following development of arthropathy bowel symptoms usually subsided as most infections are self limited. It is true that seronegative arthropathy also have strong association with Inflammatory bowel diseases (IBD) like Ulcerative colitis (UC) & crohns disease (CD). Study yielded that prevalence of spodyloarthropathy including ankylosing spondylitis in Crohns and Ulcerative colitis is 20 an 12 percent respectively. Search for association between gut and rheumatological disorder is very old. Once rheumatoid arthritis was considered as septic disease, gut and tonsil were considered as the foci of sepsis. There are report of high frequency of inflammatory gut lesion in patients with Ankylosing Spondylitis. Inflammatory lesions in the gut indeed increased the permeability and increased antigen processing by large gut in patient with Ankylosing Spondylitis. The role of gut in
the development of Ankylosing spondylitis is reflected in its treatment strategy and gut lesion also have prognostic implication in addition to etiopathogenesis. It is also found that significantly more patient with histological gut lesion needs more sulphasalazine than with normal histology. Despite of proven association between gut inflammation and spondyloarthropathies, document are sparse about the plight of gut in a symptomatic bowel. So the aims of this study is to see any colonoscopic and/ or histological abnormality in patients with ankylosing spondylitis having normal bowel habit.

**Material and Methods**

Thirty eight consecutive patients with ankylosing spondylitis of both sexes were enrolled in this observational study. This study is carried out in the rheumatological wing of the department of medicine in collaboration with department of gastroenterology and pathology, BSM medical university, Dhaka and study continued from November 2000- to October 2001. The patients were selected on the basis of revised New York criteria (1984) for ankylosing spondylitis and having normal bowel habit. Less than three motion in a day or more than three motions per week is considered as normal bowel habit.

1. **Clinical criteria**
   a) low back pain and stiffness for more than three months which improve with exercise, but not relieved by rest.
   b) limitation of motion of lumbar spine in both Sagittal and frontal planes.
   c) Limitation of chest expansion relative to normal value corrected for age and sex

2. **Radiological**
   Radiological scoring and grading of Sacroiliac joints
   Grade 0- normal
   Grade 1- suspicious change
   Grade 2- Minimal abnormality; small localized area with erosion or sclerosis without Alteration in joint width.
   Grade 3- Unequivocal abnormality; moderate or advanced sacroiliitis with one or more of followings; erosions, sclerosis, widening, narrowing or partial ankylosis.

Grade 4- Severe abnormality; total ankylosis.

If at least one clinical critera is associated with bilateral grade=2 or unilateral grade ≥3 sacroiliitis is labeled as ankylosing spondylitis. Patients taking currently DMARDs for more than three weeks, history of recent diarrhea or dysentery and who are unwilling to participate were excluded from this study. Detailed history and thorough physical examination has been done and were recorded in a predesigned data collection sheet. After obtaining informed consent all patients were subjected to full colonoscopy with biopsy.

**Colonoscopic assessment**

- Macroscopic lesions were graded as
  - Grade 0- normal
  - Grade-1- Redness and edema of mucosa
  - Grade-2- small ulceration
  - Grade-3- Mucosal edema, ulceration and hemorrhage

Full colonoscopy were performed and 10 pieces of biopsy material were taken every two pieces from each location of rectum, pelvic colon, colon descends, transverse colon and colon ascends and caecum. Bowel preparation has been done using 20% mannitol and tab laxenna.

**Histological assessment**

Histolgical features were graded as below-
- Grade-0- normal- low number of lymphocyte and plasma cell in the lamina propria, no or few Granulocytes.
- Grade-1- Slight invasion of plasma cell and/ or lymphocytes or occasional granulocytes in the lamina propria.
- Grade-2- Moderate to severe inflammation, abundant lymphocytes and plasma cell and infiltration of granulocytes in crypt.
- Grade-3- Partial glandular atrophy, crypt dilatation, and microgranuloma in lamina propria.

Data were analyzed with statistical package for social science (SPSS). Frequencies of macroscopic and microscopic lesions were calculated as percentages, and other data expressed as mean and standard deviation.
### Results
Thirty eight patients of ankylosing spondylitis with normal bowel habit were studied with full colonoscopy with biopsy. The age range of patients were 19-42 with mean age 26.78±6.40 and male: female ratio 32:6. Out of 38 enrolled patients, most of all have insidious disease onset (89.28%) and both axial and peripheral joint involvement (64.28%) (Table-1). All patients were undergone full colonoscopy and only 3 (7.89%) patients have some sort of naked eye abnormalities (Table2). Histopathological examination of biopsy materials have been done and indeed six (15.78%) patients showed inflammatory abnormalities of different grade (Table2). Correlation of macroscopic findings of colonoscopy and histological pictures of biopsy materials are also been assessed. (Table3). Agreement between Macroscopic and microscopic lesion were poor (κ=0.14).

#### Table 1: Demographic and clinical characteristics (n=38)

<table>
<thead>
<tr>
<th>Male : female</th>
<th>32:6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>19-42(26.78±6.40)</td>
</tr>
<tr>
<td>Mode of onset</td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>4(10.52%)</td>
</tr>
<tr>
<td>Insidious</td>
<td>34 (89.47%)</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>1-9years</td>
</tr>
<tr>
<td>Joint involvement</td>
<td></td>
</tr>
<tr>
<td>Axial</td>
<td>16(42.10%)</td>
</tr>
<tr>
<td>Axial and peripheral</td>
<td>22 (57.89%)</td>
</tr>
<tr>
<td>Enthesopathy</td>
<td>9(23.6%)</td>
</tr>
</tbody>
</table>

#### Table 2: Incidence of macroscopic and microscopic lesions (n=38)

<table>
<thead>
<tr>
<th>Macroscopic lesions (n=3)</th>
<th>No of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade0</td>
<td>35</td>
<td>92.10%</td>
</tr>
<tr>
<td>Grade1</td>
<td>2</td>
<td>5.26%</td>
</tr>
<tr>
<td>Grade2</td>
<td>1</td>
<td>2.63%</td>
</tr>
<tr>
<td>Grade3</td>
<td>0</td>
<td>0.00%</td>
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<table>
<thead>
<tr>
<th>Microscopic lesions (n=6)</th>
<th>No of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade0</td>
<td>32</td>
<td>84.21%</td>
</tr>
<tr>
<td>Grade1</td>
<td>4</td>
<td>10.52%</td>
</tr>
<tr>
<td>Grade2</td>
<td>2</td>
<td>5.26%</td>
</tr>
<tr>
<td>Grade3</td>
<td>0</td>
<td>0.00%</td>
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#### Discussion
This observational study was done with an intension to see the inflammatory gut lesions in ankylosing spondylitis patients having normal bowel habit. Histology of colonic mucosa of healthy Bangladeshi was not greatly different from that of western population excepting the presence of mild eosinophilic infiltration. Higher frequencies of worm infestation or unknown food allergies could be the possible explanation. In a prospective study done by Mielants et al., they had performed total colonoscopy in 211 patients (75 AS, 32RA, 104 undifferentiated spondyloarthropathies) and 65 control. Gut lesions were present in 30% (24/75) of ankylosing spondylitis patients and none of the control. They included the patients irrespective of bowel symptoms. In another study Simenon et Al found macroscopic gut lesion in 37.5% of patients. They also included patients of both symptomatic and normal bowel habit also. In our series we enrolled the patients having no bowel symptoms and with ankylosing spondylitis. Here it is found that 7.89% (3/38) patients showed macroscopic lesions (Grade1 &2) on colonoscopy and 15.87% (6/38) patient depicted evidence of non-granulomatous chronic inflammatory lesions microscopically (Grade1 &2). So this finding did not conform well with earlier studies aforementioned. This low frequencies of both macroscopic and microscopic lesions can be anticipated as here we had taken only normal bowel habit patients. In developing countries infective bowel lesion including bacterial and parasitic are common. So this minimum bowel abnormalities may not have any relation with such sero-negative rheumatic disease. In a study De vos et al showed long term evolution of gut inflammation in patients with spondylo arthropathy and found 29% patients reporting complaints of mild diarrhea and they found
evidence of chronic inflammation in 35% patients without intestinal symptoms. Our finding was much less than this study. From this study we can come to a conclusion that gut inflammatory lesions in ankylosing spondylitis patients with normal bowel habit is not remarkable. So before making concrete opinion, further large sized comparable study with & without bowel symptoms can be warranted.

References

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