Association of Inflammatory Pathologies and Crohn's Disease: A Retrospective Study in the West Algerian Region

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ABSTRACT

Background: Crohn’s disease is a chronic and recurrent inflammatory bowel disease that progresses slowly. Also CD patients have a large number of extra-intestinal manifestations.

Objective: we sought to define the possible associations between inflammatory pathology and localization and on the other hand, inflammatory pathologies and the disease behavior

Methods: A retrospective analytical study was carried out at the level of gastric and general surgery services of Western Algerian University Hospital of Sidi Bel Abbes region, during the period 2007-2019.

Results: Our study was based on a total sample of 295 cases involving 114 females (38.6%) and 181 males (61.4%) with a sex ratio of (1.58). The location of the disease at the time of diagnosis was dominated by the ileo-caecal location (55.3%), of which 64.4% were associated with inflammatory pathology (IP). The majority of patients diagnosed with Crohn’s disease had an inflammatory behavior and this for all age groups. The appendix, the ulcer and inflammatory anemia are most associated with Crohn’s disease. For inflammatory extra-intestinal manifestations, only group of patients with arthralgia had significantly higher rates in the 20-60 age groups. The mainly noted risk factors were appendectomy with (17.3%), smoking (22.4%) with a highly significant association, and alcoholism (6.1%).

Conclusion: According to our results the association of inflammatory pathology and crohn disease is more frequent in male and dominated by arthralgia as extra-intestinal manifestations lesions.

Keywords: Crohn disease; Inflammatory pathology; disease behavior; inflammatory extra-intestinal manifestation.

INTRODUCTION:

Crohn’s disease (CD) is a chronic and recurrent inflammatory bowel disease that progresses slowly and is characterized by an inflammatory exacerbation and regression. Patients may develop one or more phenotypes during the course of their disease, and often progress from inflammatory disease to severe complications. Unfortunately, there is no cure for CD and most patients need at least one surgical resection.

In addition, patients suffering from other gastrointestinal diseases may also have a large number of extra-intestinal manifestations, the main symptoms of which affect the musculoskeletal system. It is hypothesized that lymphocytes activated in the gut migrate to the joints and trigger the...
onset of extraintestinal manifestations in the joints. Other groups of inflammatory pathologies, such as inflammatory anemia, peritonitis, ulcer, villous atrophy and appendicitis, are seen in Crohn’s disease. These latter can occur before the actual bowel disease is diagnosed.

Certain risk factors such as tobacco, infection, pharmacological agents, stress, pollution and diet have been the most incriminated causes of these pathologies. However, some studies in the development of CD are contradictory, as some have found that appendectomy has a role in the onset and clinical course of the disease, while others have shown that there is no association between appendectomy and the development of CD.

In this study, we sought to define the possible associations between inflammatory pathology and localization and on the other hand, inflammatory pathologies and the disease behavior. We also investigated whether one of the inflammatory pathologies was more likely to be associated with Crohn’s disease.

PATIENTS AND METHODS:

It was an analytical retrospective study including 295 patients diagnosed with Crohn’s disease at the level of gastrology and general surgery services of Western Algerian University Hospital “Dr. Hassani Abdelkader” of Sidi Bel region, during the period 2007-2019.

The data collection was carried out using medical records including the following medical features: age, sex, location, disease behavior, treatment, inflammatory pathologies and risk factors.

Statistical analysis:

The statistical analytical study and raw data were processed using rates and cross-tabulations. Associations between categorical parameters were tested using the Chi-square test ($\chi^2$). The results were presented using the p-value, the level of its significance was limited by the 5% rate. All data were processed and analyzed by SPSS 20.0 (Statistical Package for the Social Sciences, IBM Corporation, Chicago, IL August 2011).

RESULTS:

Our study was based on a total sample of 295 cases involving 114 females (38.6%) and 181 males (61.4%) with a sex ratio of (1.58). The age range was between 16-80 years, which represents an average of 38.91. Most of the patients were in the age group of 20-40 years (138/74) M/F. We found a significant association of 0.02 between inflammatory pathology (IP) and Crohn’s disease with a percentage of 12.8% of females and 31.9% of males (Tables 1 and 2).

The location of the disease at the time of diagnosis was dominated by the ileo-caecal location 55.3% and present in all age group. 64.4% of them were associated with IP and with a significant association (SA) of 0.004. The colonic localization detected in the age groups <20-80 years (37.6%), of which 28% were associated with IPs and with an AS of 0.003. Finally, the jejunal localization with a percentage of 7.1% was only present in the age groups 20-80 years, and only 7.6% of them were associated with IPs (Tables 1, 2).

The majority of patients diagnosed with Crohn’s disease had an inflammatory behavior (46.8%) and this for all age groups. 50.8% of them was associated with inflammatory pathologies (Tables 1, 2). Similarly, common studied population complained of occlusive syndrome (36.9%), sub-occlusive syndrome (23.4%), fistula (12.9%), and (6.4%) abscess and perineal SD (Tables 1).

We also point out that the disease can be diagnosed by biological examination and para-clinical examination.

Biological examination showed that 34.2% of men had anemia (<130g/l), however, 24.7% of women had anemia (<120g/l). The inflammatory assessment based on CRP and Vs showed that 37.3% of patients had CRP (>11mg/l) and 38% had Vs 1h (>7mm); 2h (>11mm). Serology assessment showed that 0.2% had ASCA positive, 1.7% EBV positive, 7.1% TB positive, 1.7% Cytomegalovirus, 6.8% ECB and 0.7% had Varicella zoster virus (Table 1).

The para-clinical examination study showed that 60.7% were examined by ultrasound, 59.7% holl transit, 44.7% scan, 38% radiography, 36.3% telehorax, 33.2% barium enema and 5.8% PSA. Other patients underwent endoscopic examination including 79% colonoscopy and 26.1% rectosigmoidoscopy (Table 1).

Crohn’s disease treatment is medical and often surgical, indeed, 24.1% are treated with 5-assa, of which 34.8% of its patients take 5-assa treatment combined with PIs with a highly significant association of <0.001. 13.6% of patients were treated with immunosuppressants. 6.4%, patients treated with corticosteroids and biotherapy. Only 6.1% of patients receiving biotherapy associated with IP (Table 1, 3).

Sometimes, surgical treatment becomes necessary since 29.2% of patients underwent ileo-coecal resection with ileocolic anastomosis, 13.9% right hemicolectomy, 13.6% ileal resection with ileo-ileal anastomosis, 10.5% sigmoid resection, 5.1% jeunal resection and fistula resection and finally 1.4% total colectomy (Table 1).

With regard to the association of Crohn’s disease and inflammatory pathologies, two groups have been identified that do not differ significantly with age groups, namely (Tables 1, 3):

- 7.1% have peritonitis,
- 2.4% have gastritis,
- 1.7% have ulcerativecolitis,
- 0.7% have villous atrophy and chronic bronchopneumopathy,
- 0.3% have meningitis.

And those that have a significant association with the age groups:

- 33.3% have the appendix at a significant rate (p=0.01) in the under-20 age group, however it was 66.7% in the 20-40 age group.
- The ulcer appeared with a rate of 33.3% (p=0.02) in the under-20 age group. It increased to 66.7% in the 20-40 age group.
- 66.7% for inflammatory anemia was reported in patients with disease started less than 20 years with a highly significant rate (p < 0.001).

For inflammatory extra-intestinal manifestations, we noted that only the group of patients with arthralgia (12.5%) had significantly higher rates in the 20-40 (p=0.01) and 40-60 (p=0.02) age groups; however, Ankylosing spondylitis had a rate of 7.5% and arthritis a rate of 2.4% (Tables 1, 3).

We reported as well that all patients who suffered only from Crohn’s disease had significant rates in the 20-40 year age
group (p = 0.004), 40-60 year age group (p = 0.004) and 60-80 years (p = 0.05).

The major noted risk factors were: appendectomy with (17.3%), smoking 22.4% with a highly significant association p < 0.0001 of which 26.5% are associated with IP, and the last risk factor was alcoholism 6.1% with p=0.001, of which 6.8% are associated with IP (Tables 1, 2).

Table 01 : Patients medical features

| Characteristics : | Number of cases | Percentage % |
|--------------------|----------------|--------------|
| **Gender**         |                |              |
| Female             | 114            | 38.6         |
| male               | 181            | 61.4         |
| **Age range**      |                |              |
| >20 years          | 14             | 4.7          |
| 20-40 years        | 212            | 71.9         |
| 40-60 years        | 55             | 18.6         |
| 60-80 years        | 14             | 4.7          |
| minimum age        | 16 years old   | 38.91        |
| maximum age        | 80 years old   |              |
| **Age range at presentation** |                |              |
| >20 years          | 23             | 7.8          |
| 20-40 years        | 223            | 75.6         |
| 40-60 years        | 42             | 14.2         |
| 60-80 years        | 7              | 2.4          |
| minimum age at presentation | 12 years |              |
| **Location**       |                |              |
| Ileo-caecal location | 163           | 55.3         |
| Colonic location   | 111            | 37.6         |
| Jejunal location   | 21             | 7.1          |
| **Behavior**       |                |              |
| Inflammatory.T     | 138            | 46.8         |
| Stenosing.T        | 126            | 42.7         |
| Fistula.T          | 24             | 8.1          |
| ano-perineal.T     | 7              | 2.4          |
| **Clinical feature**|                |              |
| Pain syndrome      | 19             | 6.4          |
| Occlusive syndrome | 109            | 36.9         |
| Sub-occlusive syndrome | 69         | 23.4         |
| Crohn disease      | 27             | 9.2          |
| Fistula            | 38             | 12.9         |
| Abscess            | 19             | 6.4          |
| Perineal syndrome  | 14             | 4.7          |
| **Biological examination** |            |              |
| CRP (>11mg/l)      | 110            | 37.3         |
| Vs 1h (>7mm); 2h (>11mm) | 112     | 38.0         |
## Anemia

| Male < 130g/l | 101 | 34.2 |
| Female < 120g/l | 73 | 24.7 |

### Serology

| Serology | Test | Positive | Negative | Not done |
|----------|------|----------|----------|----------|
| ASCA | | | 6 | 2.0 |
| ANCA | Negative | 2 | | 0.7 |
| | Not done | 293 | | 99.3 |
| EBV | | 5 | | 1.7 |
| TB | | 21 | | 7.1 |
| ECB | | 20 | | 6.8 |
| Cytomegalovirus | | 5 | | 1.7 |
| Varicelle zona virus | | 2 | | 0.7 |

### Para-clinical examination

| Test | Positive |  |
|------|----------|---|
| PSA  | 17 | 5.8 |
| Telethorax | 107 | 36.3 |
| Radiography | 112 | 38.0 |
| Barium enema | 98 | 33.2 |
| Hail transit | 176 | 59.7 |
| Ultrasound | 179 | 60.7 |
| Scan | 132 | 44.7 |

### Treatment

| Test | Positive |  |
|------|----------|---|
| 5-as | 71 | 24.1 |
| Immunosuppressants | 40 | 13.6 |
| Corticosteroids | 19 | 6.4 |
| Biotherapy | 19 | 6.4 |

### Operating indications

| Test | Positive |  |
|------|----------|---|
| Total coloprotection | 04 | 1.4 |
| Right hemi-colectomy | 41 | 13.9 |
| Fistula resection | 15 | 5.1 |
| Ileal resection with ileo-ileal anastomosis | 40 | 13.6 |
| Ileocaecal resection with ileocolic anastomosis | 86 | 29.2 |
| Sigmoid resection | 31 | 10.5 |
| Jejunal resection | 15 | 5.1 |
| Not done | 63 | 21.4 |

### Inflammatory pathology

| Test | Positive |  |
|------|----------|---|
| Appendix | 03 | 1.0 |
| Villous atrophy | 02 | 0.7 |
| Ulcer | 03 | 1.0 |
| Chronic bronchopneumopathy | 02 | 0.7 |
Meningitis 01 0.3
Ulcerative colitis 05 1.7
Crohn disease 90 30.5
Inflammatory anemia 03 1.0
Gastritis 07 2.4
Peritonitis 21 7.1

Extraintestinal manifestations « Inflammatory »

Ankylosing spondylitis 22 7.5
Arthralgia 37 12.5
Arthritis 07 2.4

Risk factors

Appendectomy 51 17.3
Smoking 66 22.4
Alcoholism 18 6.1

Table 02: Association with inflammatory pathology and medical features.

|                         | Associated with inflammatory pathology | Not associated with inflammatory pathology | P-Value |
|-------------------------|----------------------------------------|--------------------------------------------|---------|
| Gender (F/M)            | 38/94 (28.8/71.2)                      | 76/87 (46.6/53.4)                          | 0.002   |
| Location                |                                        |                                            |         |
| Colonic localization    | 37 (28)                                | 73 (44.8)                                 | 0.003   |
| Ileo-caecal location    | 85 (64.4)                              | 78 (47.9)                                 | 0.004   |
| Jejunal localization    | 10 (7.6)                               | 11 (6.7)                                  | 0.78    |
| Behavior                |                                        |                                            |         |
| Inflammatory.T          | 67 (50.8)                              | 71 (43.6)                                 | 0.21    |
| Stenosing.T             | 52 (39.4)                              | 73 (44.8)                                 | 0.35    |
| Fistula.T               | 08 (6.1)                               | 16 (9.8)                                  | 0.24    |
| ano-perineal.T          | 04 (03)                                | 03 (1.8)                                  | 0.50    |
| Treatment               |                                        |                                            |         |
| 5-asa                   | 46 (34.8)                              | 25 (15.3)                                 | <0.0001 |
| Immunosuppressants      | 18 (13.6)                              | 22 (13.5)                                 | 0.97    |
| Corticosteroids         | 05 (3.8)                               | 14 (8.6)                                  | 0.09    |
| Biotherapy              | 08 (6.1)                               | 11 (6.7)                                  | 0.81    |
| Smoking                 | 35 (26.5)                              | 31 (19)                                   | 0.12    |
| Alcoholism              | 09 (6.8)                               | 09 (5.5)                                  | 0.64    |
Table 03: Cumulative extraintestinal manifestations and complications in Crohn’s disease

| Characteristics | >20 | 20-40 | 40-60 | 60-80 |
|-----------------|-----|-------|-------|-------|
| Extraintestinal manifestations « inflammatory » « n (%) p » | | | | |
| Ankylosing spondylitis | 01(4.5%) p=0.9 | 18(61.8%) p=0.2 | 02(9.1%) p=0.2 | 01(4.5%) p=0.9 |
| Arthralgia | 01(2.7%) p=0.53 | 33(89.2%) p=0.01 | 02(5.4%) p=0.02 | 01(2.7%) p=0.53 |
| Arthritis | 00 (00) p=0.5 | 06 (85.7%) p=0.4 | 01 (14.3%) p=0.7 | 00 (00) p=0.5 |
| Inflammatory pathology « n (%) p » | | | | |
| Appendix | 01 (33.3%) p=0.02 | 02 (66.7%) p=0.8 | 00 (00) p=0.4 | 00 (00) p=0.6 |
| Villous atrophy | 00 (00) p=0.7 | 02 (100%) p=0.3 | 00 (00) p=0.5 | 00 (00) p=0.7 |
| Ulcer | 01 (33.3%) p=0.02 | 02 (66.7%) p=0.8 | 00 (00) p=0.4 | 00 (00) p=0.6 |
| Chronic bronchopneumopathy | 00 (00) p=0.7 | 01 (50%) p=0.4 | 01 (50%) p=0.2 | 00 (00) p=0.7 |
| Meningitis | 00 (00) p=0.8 | 01 (100%) p=0.5 | 00 (00) p=0.6 | 00 (00) p=0.8 |
| Ulcerative colitis | 00 (00) p=0.6 | 05 (100%) p=0.1 | 00 (00) p=0.2 | 00 (00) p=0.6 |
| Crohn disease | 06 (6.7%) p=0.3 | 75 (83.3%) p<0.0001 | 08 (8.9%) p=0.004 | 01 (1.1%) p=0.05 |
| Inflammatory anemia | 02 (66.7%) p<0.0001 | 00 (00) p=0.005 | 01 (33.3%) p=0.5 | 00 (00) p=0.6 |
| Gastritis | 00 (00) p=0.5 | 07 (100%) p=0.09 | 00 (00) p=0.2 | 00 (00) p=0.5 |
| Peritonitis | 00 (00) p=0.2 | 18 (85.7%) p=0.1 | 03 (14.3%) p=0.5 | 00 (00) p=0.2 |

**DISCUSSIONS:**

A total of 297 cases of Crohn’s disease were identified during the period of 2007-2019. The median age for developing Crohn’s disease was about 39 years. In the same way, studies of [7,8] showed that the median age at diagnosis of CD patients was approximately 30 years. However, in the study of [9] the patients were younger, since the minimum age of onset of the disease was 12 years.

The majority of patients were more likely males which is consistent with the results of [9,11] but not with those of [7,12].

In our study, different segments of the digestive tract were affected, but colonic and ileocecal localizations were the majority. These results are similar to those reported in different studies by (Adler et al, 2017; Can et al, 2015; Duarte-Silva et al, 2019; Herzog et al, 2018).

All age groups showed colonic and ileocecal localization, which is consistent with the results of (Herzog et al, 2010). Whereas, the jejunal localization in our study was more present in the age groups of 20-80 years. However, it was noted in the patients under the age of 40 in the Herzog study.

Our results showed that the inflammatory and stenosing phenotypes were the most frequent, followed by complicated cases of fistulas and ano-perineal lesions as confirmed by the results of several authors (Feuerstein and Cheifetz, 2017; Kugathasan et al, 2017).

The inflammatory and stenosing types affected all age groups of our population, which is consistent with the results of (Herzog et al, 2018).

Moreover, we noticed that the most common symptoms in our patients were occlusive Sd, sub-occlusive Sd, abscess and fistula, which agrees with [13] findings.

The most altered biological signs in our patients were:

- CRP >11mg/L, Vs 1h (>7mm); 2h (>11mm) with non-significant association as reported by [14,15].
- Anemia in both men (<130) and women (<120) as noticed by [16,17].
- Only 2% of the patients carried out the serological assessment with an ASCA positive for the presence of the antibodies directed against the mannans in particular the Anti-Saccharomyces Cerevisiae "ASCA".

Gologan S et al (2012) have found that the highest IgA and IgG are linked to a younger age at diagnosis and to more aggressive phenotypes in Romanian patients with CD (Huang et al, 2012).

7.1% of our patients had a positive TBC. Similarly, studies by (Rais et al, 2012) have noted that the digestive tract can also be affected by tuberculosis and considered to be a granulomatous disease. Therefore, it would be inappropriate and even dangerous to treat a patient who actually has Crohn’s disease with anti-tuberculosis therapy.

Cytomegalovirus infections were noted in 1.7% of patients, EEB in 6.8% of patients and Varicella zoster virus in 0.7% of patients as noted by (Bengi et al, 2018). Colonoscopy was the most frequent test of diagnostic with a rate of 79%, which is consistent with the results of [18].

Among the 295 studied cases; a highly significant association was found between inflammatory pathology and Crohn’s disease (44.7%). Of these, 7.1% are peritonitis, 2.4% are gastritis, 1.7% are UC, 0.7% are villous atrophy and COPD. These results are similar to those of [19,20]. We also found 0.3% cases of meningitis and 0.1% of appendicitis in the under 20 age group with a significant rate. These results have been
proven by 6.21. Other IPs were found in our study, namely ulcers that appear in the under-20 age group and inflammatory anemia that occurs at <20-40 years of age. Both with a significant association. This is consistent with the results of 7.

In order to control inflammation and to relieve pain in Crohn's disease, the first-line treatment prescribed is medication. The choice of drug and route of administration depends on the intensity of the symptoms and their location in the digestive system. In our study 24.1% of patients were treated with 5-ASA. This prescription was also noted in the study of (Liu et al., 2016). Only 13.6% of patients were treated with immunosuppressants to calm the inflammatory reactions. These drugs are generally used to maintain remission after attack therapy (Hillier et al., 2019; Liu et al., 2016). As surgical treatment 29.2% of patients underwent ileocaecal resection with ileocoeal anastomosis, 13.9% underwent a right hemi-colectomy which is in accordance with the results of 8.22.

Joint damage is the most common extra-digestive manifestation in Crohn's disease. In our study, Arthritis was the most common inflammatory extra-intestinal manifestations with a rate of 12.5%. It reaches significantly higher rates in the 20-60 age group. These results are identical to those of (Herzog et al, 2018). Other studies (Bae et al.; 2017; Herzog et al.; 2018; Hiller et al.; 2019; Hsu et al.; 2017) have shown that Crohn's disease develops signs of ankylosing spondylitis (AS) affecting joint including that of the spine. 7.5% of our patients have developed AS. However, in other studies (Bae et al.; 2017; Bandyopadhyay et al.; 2015; Subramaniam et al.; 2015), arthritis was the most reported whereas in our study we noted only 2.4% of patients developing arthritis

Crohn’s disease remains an unknown and as yet ill-defined disease, however, medical progress has made it possible to move towards the existence of other risk factors. In our study 22.4% of patients were smokers (also noticed by Bandyopadhyay et al; 2015): 6.1% of men were alcoholic and 17.3% of patients had an appendectomy. Ameta-analysis of several studies has shown that, despite the heterogeneity, there is still a higher relative risk of developing crohn’s disease after appendectomy 6.23.

CONCLUSION:
This study has shown that the association of inflammatory pathologies and Crohn’s disease is more common in males; it often affects young ages with an ileocecal location and dominated by extra-intestinal manifestations of lesions such as arthralgia.

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