Clincopathological Assessment of Cases of Inflammatory Bowel Disease & Other Types of Colitis in Province of Basrah

Russul Mahmood Ali*, Alaa G Hussein**

ABSTRACT:

BACKGROUND:

Inflammatory bowel disease is group of inflammatory disorders of unknown etiology. The main members of this group are ulcerative colitis and Crohn's disease (granulomatous colitis).Histopathologic evaluation of colonoscopic mucosal biopsy remains one of the earliest modalities of investigation in patients which clinically suspected. Any biopsy underwent histopathological diagnosis should be accompanied by endoscopic findings and full clinical history.

OBJECTIVE :

Assessment of colonic biopsies in patients of colitis on the basis of specific histopathological criteria and correlation with clinical and endoscopic presentations.

METHOD :

A Retrospective and prospective study included randomly selected 102 colonic specimens from January 2016 to June 2018.The clinicopathological parameters including (age of the patients, gender, hematochiza, diarrhea and abdominal pain) obtained from endoscopic reports and correlated with the histopathological parameters and sections which revised by a senior pathologist.

RESULTS:

Out of (102) patients in this study; there were 41(40.2%) males and 61(59.8%) females. hematochiza is the main presentation in ulcerative colitis, while abdominal pain is the main presentation in Crohn's disease patients and diarrhea in those with non-specific colitis. Certain parameters can favoring the diagnosis of non-specific colitis over inflammatory bowel disease and another set favoring ulcerative colitis over Crohn's disease and vice-versa. This leads in shifting of diagnosis of most of endoscopic biopsies rather than resection biopsies. And there is under diagnosis of cases of non-specific colitis and Crohns disease in comparism to Ulcerative colitis.

CONCLUSION:

Inflammatory bowel diseases are female predominate.Ulcerative Colitis predominate in 3rd and 4th decades of life, Crohn's disease is more in 2nd and 3rd decades while non specific colitis are more found in old age. Correlation between clinical, endoscopic and histopathological features is essential in the diagnosis of inflammatory bowel diseases. Accurate diagnosis of inflammatory bowel diseases depends on finding of certain histopathological features.

KEYWORDS: Inflammatory bowel diseases, Ulcerative Colitis, Crohn's disease, histopathological features diagnostic of IBS, granulomatous colitis.

INTRODUCTION:

Inflammatory bowel diseases are of unknown etiology but suggest genetic susceptibility and environmental exposure lead to inappropriate immune response to enteric mictobiota leading to characteristic inflammatory lesion of the GIT[1]. The diagnosis depend on combination of medical history ,clinical examination, laboratory data (negative for stool examination for infectious agent[2] , endoscopic , radiologic and histologic finding.[3,4]

* Dept. of Pathology, Laboratories of Al-Imamain Al-Kadhumain Medical city, Baghdad, Iraq.

**Dept. of Pathology and Forensic Medicine, College of Medicine, Al-Nahrain University, Baghdad, Iraq.

1-Ulcerative colitis involve the mucosa and submucosa[3], and limited to colon and rectum[5].
Acute stage: increase number of inflammatory infilterate in lamina propria including basal plasmacytosis, crypt abscess preceding by accumulation of neutrophils at the base of the crypts[6] which lead to progressive destruction of crypt , decrease cytoplasmic mucus and irregular shapes crypts (from atrophic and regenerative changes), goblet cells dysplasia and crypt architecture distortion[7]
Ulcerative colitis is a disease of continuity i:e has a continuous fashion not a ship lesion like Crohn's disease ,has remission and relapse phase[8].
Grossly: vary with disease stage:
Acute stage: the mucosa of the bowel is wet and shine from blood and mucus with petechial hemorrhage , ulcers of different size and shapes then appear(6), red sessile nodules known as "pseudopolyps".
Advanced stage: the bowel is fibrotic , narrow and short.The stenosis associated with inflammatory mass may be mis-diagnosed clinically and radiologically as carcinoma[9].Quiescence stage: the mucosa may appear grossly narrow with absence of ulceration , the wall is atrophic and submucosal fat deposition [10].
2-Crohn's disease involve any part of GIT from mouth to anus , but mainly the terminal ilieum (regionalenteritis)[11], typically transmural ,the pathogenesis depend largely on genetic sustibility and bacterial infection (microbme)[12].
Grossly(10): - skip lesions (segmental involvement of the bowel) with cobble stone appearance,usually associated with stricture formation and fissuring, the fissures by short transverse ulcers which when healed give rail- track scars appearance.
Microscopically(9): - fissuring , non caseating granuloma in 40 – 60 %of cases and transmural involvement is the typical feature of Crohn's disease. The mucosa has well defined fociof inflammatory cells surrounded by normal non inflamed mucosa → suggestive of Crohn's disease.
- The main histological features to look for is granuloma which may need serial sectioning, patchy mucosal involvement with inflammation, pyloric cells metaplasia and goblet cells preservation[13] .The ilieum may be involved in about 50% of cases(14).
Anal lesions in 75% of cases (with fissure, fistula , ulcerations) may appear as first manifestation of Crohn's disease, enlarged regional lymphadenopathy which microscopically not differentiated from ulcerative colitis only by the presence of granuloma[15].Internal fistula is pathognomonic of Crohn's disease [14].
3-Indeterminate colitis: when most of the features are not pathognomonic for either disease , so term indeterminate colitis applied to such cases ; which later mostly develop ulcerative colitis rather Crohn'sdisease[16].
- Clinico-patholologic parameters involved in histopathological evaluation of cases of inflammatory bowel disease and other types of colitis(2):
A- Clinical presentation of patients(Bleeding per rectum, Diarrhea, Abdominal pain, Perforation, Anal complication, Intestinal obstruction, Fistula)
B-Microscopically:
1.Distribution of involvement.
2. Mucosal atrophy and regeneration
3. Cytoplasmic mucin
4. Edema
5. Granulomas
6.Fissuring
7.Cryptabscess
8.Rectalinvolvement
9.Ilealinvolvement
10.Lymph node status(hyperplasia, confluent, germinal center formation, granuloma)
11. Crypt architecture (normal, mild distortion, moderate distortion, marked distortion)
12. Goblet cells (focal, diffuse) loss.
13. Cryptitis.
14. Activity of disease (mild, moderate , sever).
15. Dysplasia
16. Basal plasmocytosis and lymphoplasacytosis
17. Dense chronic inflammation of lamina propria , lymphoidaggregate
18. Pseudopolyps formation
19. Transmural involvement
20. Paneth cell metaplasia of left colon.

METHODS:

A Retrospective and prospective study of randomly selected 102 colonic specimens (surgically resected and endoscopic colonic biopsies) were collected at Teaching Laboratories of Al-Basra Teaching Hospital and Private laboratories from January 2016 to June 2018.
This study concentrated on collecting all types of colitis and inflammatory bowel disease in order to re-evaluate and correct assessment of their histopathological diagnosis.

Features in association with their clinical presenting symptoms were obtained from archives in hospitals and from the laboratories pathological reports.

The clinicopathological parameters including (age of the patients, gender, bleeding per rectum, diarrhea, abdominal pain and histopathological features) were obtained from patients' pathological requests and hospital's archives.

The practical work up include randomly collected 102 colonic formalin fixed paraffin embedded tissue block(biopsies and surgical resected) these cases were diagnosed as(non-specific colitis, Ulcerative colitis (active) with or without dysplasia, suspicious Ulcerative colitis, Crohn's disease, suspicious Crohn's disease, Normal biopsy). Re-blocking, sectioning, H&E staining was conducted. From each block a 3 mm thickness section was taken and stained with routine H&E stain.

H&E stained slides were examined and re-evaluated by pathological specialist and the revision of the histopathological diagnosis according to certain histopathological parameters.

Features favering IBD over non specific colitis(2):

A. Highreliable:
1- Basal plasmacytosis(focal or diffuse)
2- Crypt atrophy
3- Crypt distention / branching /abnormal architecture.
B.Fairlyreliable:
1-Granulomas.
2- Basal lymphoid aggregates(which should be differentiated from normal lymphoid aggregate)
C. Less reliable:
1- Lamina propria is chronically inflamed and hyper cellularity.
2- Paneth cell metaplasia (nonspecific distal to splenic flexure).
3- Deep rather than superficial crypt abscess.
4- Variable crypt diameters.
5- Crypt intra epithelial neutrophils or luminal neutrophils.

Features favering other colitis types over IBD(2):

A. More reliable:
1. Absence of features of IBD
2. Preservation of crypt architecture.
3. Parallel crypt and no branching.
4. absences of basal plasmacytosis.

B.Lessreliable:
1- inflammation in upper half of lamina propria.
2- hyper cellularity of upper two third of mucosa.
3- acute inflammation rather than mixed chronic inflammation in lamina propria.
4-cystic crypt abscess.

Features favering ulcerative colitis over Crohn's disease(2):

A.Reliable:
1-diffusecryptabnormalities
2-cryptatrophy
3-abnormal crypt architecture
4-mucin depletion
5-absencesof ileal inflammation

B.Lessreliable:
1- distal rather than proximal diffuse mucosal inflammation.
2-diffuse crypt changes.

Features favering Crohn's disease over ulcerative colitis(2)s:

A.Reliable:
1. Transmural inflammation in resection specimens.
2.granuloma (non cryptolytic)
3.2-focal or patchy lamina propria chronic inflammation.
4.focal or segmental crypt distortions.
5-Ilealinvolvement.
6-absence of features of ulcerative colitis.

B.Less reliable :
1- Focal crypt abscess /or focal cryptitis.
2-Segmental crypt atrophy.
3-Segmental mucin depletion

Statistical analysis: we start statistical analysis by using the mean and standard deviations, frequency, bar and pie chart.

RESULTS:

Of 102 colonic biopsies(19 resection colonic specimens and 83 endoscopic biopsies) diagnosed primarily as(33 cases Non-specific colitis, 24 cases ulcerative colitis (active) with or without dysplasia, 15 cases suspicious ulcerative colitis, 9 cases Crohn's disease, 9cases suspicious Crohn's diseas and 12 Normal case. After the application of previous histopathological parameters and correlations with clinical aspects; there are shifting in the diagnosis as shown in table (4. 1). The shifting in the diagnosis shows that mostly involve the endoscopic rather than the resection

specimensand there is under diagnosis of cases of non-specific colitis and Crohn's disease this is probable due to need a resection biopsies for diagnosis rather than endoscopic ones.

Table 4.1: The histopathological diagnosis and percentage before and after application of histopathological Parameters with percentage of shifting in diagnosis.

Histological diagnosis	No. of cases in preliminary diagnosis	percentage of cases in preliminary diagnosis	No. of cases afer application of the parameters	Percentage of cases afer application of the parameters	Percentage of shifting
Non-specific colitis	33	32.3 %	52	51%	+18.7%
Suspected Crohn's disease (probable)	9	8.8%	5	4.9%	- 3.9%
Crohn's disease	9	8.8%	13	12.7%	+ 3.9%
Suspected ulcerative colitis (probable)	15	14.7%	10	9.9%	- 4.8%
Ulcerative colitis	24	23.5 %	19	18.6%	- 4.9%
Normal	12	11.9 %	3	2.9%	- 9 %
Total NO.	102	102			

According to age: the mean age for male with non-specific colitis 6.2 years and for females5.7 years, for male with ulcerative colitis = 3 4.1 years and for females 5.5 years, for male with Crohn's disease is years and for females 5.1 years. Among the (102) patients who had either endoscopic or excisional biopsies from the large bowel, there were (41) males (40.2 %) and (61) females(59.8%).

The patients with non-specific colitis ; the male to female ratio is approximately (1 : 1), for ulcerative colitis ;the male to female ratio is (1 : 3) and (1:2)for Crohn's disease patients.

☒ The sex distribution of these patients with various types of colitis and IBD is shown in table (4.2).

Male	Female	Male:Female ratio	
Non-specific colitis	22	30	≈ (:)
U.C	8	21	(1:2.6)
Crohn's disease	8	10	(1:1.25)

The clinicopathological parameters include first bleeding per rectum which is out of the (47)cases of IBD collected during the study ,there were (32)cases (68.1%) of cases present with bleeding per rectum , while [15] cases (31.9%) were free . Among those cases that present with bleeding per rectum [16]cases (50%) had active ulcerative colitis, (9) cases (28%) were diagnosed as probable ulcerative colitis ,(3) cases (9.5%) were suspected Crohn's disease and (4) cases (12.5%) were Crohn'sdisease.

The second parameter included in this thesis is abdominal pain :out of the (102) cases collected for the study ,(85) cases were found to be present with abdominal pain in their pathological requests.

From those (102) cases it was found that out of them (49) cases (57.6%) were non-specific colitis, (14) cases (16.5 %)were Ulcerative Colitis patients active disease,(7) cases (8.2%) were suspected ulceratives, (11) cases (13%) are active Crohn's and (4) cases (4.7%) were suspected Crohn's disease.

The third and last parameter is diarrhea: the frequency of diarrheal presentations was (45)cases (44.1 %) in nonspecific colitis , (10) cases (9.8%) in ulcerative colitis , (3) cases (2.9 %) in Crohn's disease and (44) cases are free (43.2%) from diarrhea.

Table 4.3: The numbers and percentage of cases with diarrheal presentation.

NO. of cases	The percentage	
Non-specific colitis	45	44.1 %
U.C	10	9.8%
Crohn's disease	3	2.9%
Free from diarrhea	44	43.2%

Figure (4.1) Non-specific colitis with superficial mild inflammation , no glandular distortion or mucindepletionx10,H&E.
Figure (4.2) Non-specific colitis with mild chronic inflammatory cell infiltrate (black arrows) x40, H&E.
Figure (4.3) Crohn's disease of the colon showed transmural inflammation with multiple non caseating granulomas (black arrows) H&E ,X10 Figure (4.4) Crohn's disease of the colon show epitheliod granuloma (black arrow) with inflammatory cell cuff X 40,H&E. Figure (4.5) ulcerative colitis of colon (acute stage) there is glandular architectural distortion(black arrows), sever mucosal inflammation , basal plasmacytosis and surface ulceration X10, H&E. Figure (4.6) ulcerative colitis of colon showing gland distortion mucin deplation (black arrows) ,H&E , X40 Figure (4.7) ulcerative colitis of colon showing mucin deplation and focal cryptitis (black arrows)X40,H&E.

DISCUSSION:

From all (102) cases of colonic biopsies (endoscopic and resection specimens we found that most shifting in the diagnosis involving the endoscopic rather than resection ones. Colorectal biopsies are widely used and are regarded a helpful tool for the differential diagnosis of various types of colitis and differentiating between types of inflammatory bowel disease (Crohn's disease and Ulcerative Colitis) and between inflammatory bowel diseases and non IBD[17].

The diagnosis of each case represents a set of variable rather than single criteria. In present study disclosed that certain histological features including (crypt atrophy, crypt distortion, basal plasmacytosis) are significant in the diagnosis of IBD and discrimination of IBD from non IBD colitis.

And the above criteria are reliable enough to apply on each given specimen to diagnose them into definite IBD and definite non IBD.[18] While discrimination of Crohn's disease from Ulcerative Colitis need several features (crypt atrophyand distortion , mucin depletion , focal inflammation , cryptitis and crypt abscess) when (cryptitis , crypt atrophy , and crypt abscess are regarded as features of Ulcerative Colitis rather than Crohn's disease.

In the other hand Crohn's disease regarded when segmental or focal distribution of the disease and focal or patchy transmural inflammation [19,20] in addition to sarcoid like granuloma which is specific for Crohn's disease [19] (definite Crohn's disease).

Our hypothesis support that certain histopathological features together with the distribution of these features around the large bowel provide better discrimination between Crohn's disease and Ulcerative Colitis and between IBD and non IBD colitis ; which seem to be efficient and sensitive to be applied in practical work[17].

In the current study, patients with ulcerative colitis were less than years and patients ≥ years; whereas (7) patients less than 35 years with Crohn's disease and ( ) patients ≥ years This is in agreement with a study in Stockholm[21] which conclude that more effection with Ulcerative Colitis occur in the 3rd and 4th decades but differ with our study in gender effected which has more male predominance.

And also in agreement with study carried in Brussels; by Van Gossum et al[22] that found that the median age for Crohn's disease is 34 years and 38 years for Ulcerative Colitis and the peak age is between 20-29 years with male to female ratio = 0.4 for Crohn's disease and 1.9 for Ulcerative Colitis but this differ with our research study regarding Ulcerative Colitis[22] which may occur due to different sample size in both studies. A Turkish study carried by Tozun et al[23] shown that a male predominance is observed in both disease and age of patients showed a characteristic biphasic distribution with a two peaks between 20-30 and 50-70 years for both sexes; while in Uruguay a study done between 2007 -2008 by Bnenavida et al[24] found that the average age of inflammatory bowel diseases is 40.7 years and no

stastically significant difference between Ulcerative Colitis and Crohn's disease in age or gender[24].

This difference could be attributed to different racial groups , different sample size , inclusion or exclusion criteria in their study.

Regarding clinical presentation for patient with IBD (bleeding per rectum , diarrhea, abdominal pain) we found that approximately two thirds of patient with IBD included in this study (32 out of 47)presents with bleeding per rectum ; and (36 out of 47)present with abdominal pain and (13 out of 47) present with diarrhea.

A study carried in Saudi Arabia by Al-Saleem K.[25] found that Ulcerative Colitis patients with 90% bleeding per rectum followed by diarrhea 86% and abdominal pain 62% and this is parallel with our study; while a study done in Bahrin by Isa HM[26] found that most patients with Crohn's disease present with recurrent abdominal pain and weight loss and this go with results we obtained in this research. Another study in North France done by Fumeny M[27] found that colitis present with 93% chronic diarrhea , 47% with abdominal pain and this agree with our results.

In Iran a study done by Aghuzadeh R[28] et al shown that most patients with Ulcerative Colitis present with bleeding per rectum (41.9%) where as those with Crohn's disease complain of abdominal pain (46.9%)(28) Inconsistent with our study in Jamica by Penn KA et al[29] whose found the main presentation of inflammatory bowel diseases is diarrhea 93%, rectal bleeding 56% , abdominal pain 48%, weight loss 25% in addition to other manifestations.

And the same results obtained from a study in India [30] shows no great difference in presentations between Crohn's disease and Ulcerative Colitis; presentations with blood in stool in 90.3% , diarrhea in 69.9% in Ulcerative Colitis whereas abdominal pain 73.8% is common in Crohn's disease[30].

From the above results we see that patients with Ulcerative Colitis most commonly presents with bloody diarrhea and bleeding per rectum while patients with Crohn's disease usually presents with abdominal pain and chronic diarrhea as predominant clinical features [31,32].

The clinical presentation of Crohn's disease and Ulcerative Colitis are similar between developed and developing countries.[33]

Also the previous presentations can't always results in diagnosis of IBD , it also can be found in other types of colonic lesion e. gpolyps, colitis, carcinomas[34,35]

CONCLUSION:

1. Inflammatory bowel diseases are presenting in both sexes with female predominance.
2. Ulcerative Colitis predominate in the third and fourth decades of life , Crohn's disease is more common in2ndand 3rd decades while non specific colitis are more found in old age groups.
3. Correlation between clinical, endoscopic and histopathological features is essential in the diagnosis of inflammatory bowel diseases.
4. Efficient diagnosis of inflammatory bowel diseases depends on finding of certain histopathological features on each given colonic biopsy.
5. Many of the colonic biopsies preliminary diagnosis changed after application of the given parameters

which effect on the mode of treatment, management and prognosis of patients.

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