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SIGNIFICANCE OF ENDOSCOPY/COLONOSCOPY VERSUS MICROSCOPY IN PATIENTS WITH CHRONIC DIARRHEA

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ABSTRACT

Objective: To know the relative significance of endoscopy/colonoscopy and microscopy in patients presenting with chronic diarrhea.

Material and Methods: Between May 2012 and September 2013 about 90 patients with chronic diarrhea turning up at Gastroenterology Department (major study group) of Hayatabad Medical Complex (HMC) and Post Graduate Medical Institute (minor study group) Lady Reading Hospital, Peshawar (PGMI, LRH), were selected as a study group. These included patients with an age range of 1.5 years to 80 years and with a mean age of 27 years. Biopsies were obtained from both the visibly normal as well as affected portions of the intestine in all these patients. The patients were, therefore, categorized into groups on the basis of gender and the procedure they had undergone. All had undergone either endoscopy or colonoscopy. The results of the two procedures (endoscopy or colonoscopy) were then mutually compared with microscopy of the biopsies.

Results: Fifty-three (58.89%) were having grossly normal-appearing mucosa on endoscopy/ colonoscopy, while the remaining patients 37 (41.11%) showed some abnormality on inspection. In contrast to this, the grossly normal-appearing mucosa on endoscopy/colonoscopy was actually not as normal on microscopy as might have been thought. On microscopy (histopathology) only 6 (6.67%) were normal. In the rest of 84 (93.33%) patients some degree of abnormality was observed.

Conclusion: These findings are clearly suggestive of the relative more importance of performing random biopsies even in macroscopically normal appearing small intestine and colon and hence suggestive of the relatively more importance of microscopy over endoscopy/ colonoscopy in diagnosis of chronic diarrhea.

Key Words: Chronic, diarrhea, Microscopy, Endoscopy, Colonoscopy.

INTRODUCTION

Chronic diarrhea remains a common nuisance among patients presenting with signs and symptoms of the gastro-intestinal tract. Some may turn up with chronic watery diarrhea but with no other specific clinical or laboratory findings. Although endoscopy/ Colonoscopy now-a-days are regarded as one of the most vital clinical aid to help in the correct diagnosis as well as management of many diseases like chronic diarrhea. However microscopy of the biopsies, provide even a more reliable and correct diagnostic tool of the disease required for proper management of these diseases. Diarrhea, in generality, may be defined in terms of stool frequency, consistency, duration and volume or weight. Patients' conceptions of diarrhea often focus around stool consistency[1]. According to World Health Organization (WHO) diarrhea is defined as having three or more loose or liquid stools per day, or as having more stools than is normal for that person[2]. Diarrhea may result from either increased secretion of fluid into the intestine, reduced absorption of fluid from the intestine or rapid passage of stool through the intestine. On the basis of duration of the disease, stool consistency and part of intestine involved. Following are the common types of diarrhea.

Acute and chronic diarrhea, small and Large bowel diarrhea, the main causes of chronic diarrhea seem to depend on the socioeconomic status of the population[7,8]. In less developed countries, chronic bacterial, mycobacterial, and parasitic infections are the most common causes of chronic diarrhea; functional disorders, inflammatory bowel disease, and malabsorption (from a variety of unspecified causes) are also common in this setting[9,10].

Chronic Diarrhea may be infective or non infective in nature. Infective causes of diarrhea are Bacteria, Parasites, Viruses,Unknown causes. Non-infective causes of chronic diarrhea are Intestinal disorders, Diarrhea due to Immune dysfunction, Drugs e.g. antibiotics, laxatives. Certain foods and food additives intolerance (e.g. cow's milk soy, protein, sorbitol, fructose, olestra), previous surgery or radiation therapy of the abdomen or gastrointestinal tract, certain Tumors e.g. Hormone-producing

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(neuroendocrine) tumors (e.g., serotonin), decreased blood flow to the GIT also called Ischemic bowel disease[14].

Patients with chronic diarrhea often present with difficult diagnostic problem. Blood or stool tests are routinely advised. For stool assessment the main stool characteristics, i.e., watery, bloody, and fatty diarrhea are required to be noted[14]. Additional tests may be required if these early tests do not disclose the cause of the diarrhea. These include radiography or X-rays, endoscopy and microscopic examination of biopsy specimens. Although endoscopy/colonoscopy is frequently performed in these patients, their usefulness with biopsy in this setting is uncertain[16,17]. Upper endoscopy has become the standard method for obtaining biopsy specimens from the upper small intestine[18].

Diarrhea in infants, moderate or severe diarrhea in young children, diarrhea accompanied by blood or the one that lasts for more than two days should be further investigated. Similarly diarrhea in cooks (food handlers), in travelers or in the one associated non-cramping abdominal pain, fever, weight loss. A severity score is applied to assist diagnosis in children[19].

The upper gastrointestinal flexible fibreoptic endoscope was first used in 1968 and proved to be a major step forward in the diagnosis of esophago-gastro-duodenal lesions[20]. Endoscopic screening may detect esophageal, gastric or intestinal mucosal lesions at an early stage especially mucosal atrophy, metaplasia and dysplasia so as to avoid development of these lesions to invasive cancer[21,22]. Diagnostic endoscopy is an invasive technique but has proved to be a simple, safe and well tolerated procedure[23].

If the patient has started receiving treatment and the severity of disease has lessened to some extent and the patient is painless, then a full colonoscopy can safely be performed. However, it is important to bear in mind, that medications can potentially alter the natural endoscopic appearance of the patient's colon[24].

MATERIAL AND METHODS

This is a comparative prospective cross sectional study. About ninety endoscopic/ colonoscopic biopsies were collected from the gastroenterology wards of the two tertiary care hospitals (HMC and PGMI LRH) of Peshawar between May 2012 and September 2013 and were studied in the department of Pathology, Hayatabad Medical Complex Peshawar. The patients included were of all age groups and from both sexes.

Those having undergone biopsy for chronic diarrhea were having an age range from 1.5 years to 80 years and with mean age 27 years. The relevant clinical information was obtained from the gastroenterology wards and laboratory request forms. The gastrointestinal symptoms included vomiting, abdominal pain/ epigastric pain, diarrhea, mucous, bleeding Per Rectum/ Rectal bleeding, anemia, polyp and weight loss.

The patients were planned for small intestinal endoscopic examination by Olympus models GIF-130, GIF-140, GIF-160 and GIF-180 endoscopes, routinely used in gastroenterology ward of HMC Peshawar. Similarly patients were prepared for colonoscopic examinations using Olympus models CF-130, CF-160, CF-180 NBI (Narrow Binding Image) and CFS-140 for children. The tissues were fixed in formaldehyde, and routinely processed in an automatic tissue processor (Model Citadel-1000, Shandon) for 17 hours and then embedded in paraffin using the embedding machine (Model Thermo Histocentre-3) in histopathology department of HMC Peshawar. Three to six sections (about 05 to 10 microns each) were cut on microtome (Model AS 325, Shandon) and routinely stained with Hematoxylin and Eosin (H&E). The tissue blocks were sectioned serially. Deparaffinization is done by incubating at 65° C for 30 minutes. Then immerse the tissue in xylene for 30 minutes. Repeat immersion in fresh xylene for another 30 minutes. The procedure adopted for H & E stain included projecting the specimens progressively first through absolute alcohol for 10 minutes, then 90% alcohol for 05 minutes, then 80 % alcohol, 70% alcohol and 50% alcohol for 01 minutes each. Then wash with tape water and after wiping the water put it in 200 ml of hematoxylin stain and incubate at room temperature for 05 minutes. Then wash in tape water from the reverse side and pass it in acid water, then put it in 400 ml of Eosin stain for 30 seconds and again wash it with tape water from reverse side. Put it again in 70% alcohol, then 80% alcohol and then absolute alcohol for two minutes each. Finally these are put in carbolic xylene and then xylene 1 and xylene 2 solution for 10 minutes each and lastly mounting of slide is done.

Most of the biopsies were taken from duodenal, jejunal, ileal and colonic mucosa. On Day 1 the patient was asked to consume only fluid diet like soup, green tea and water. On day 2 and day 3, in addition to above, he/she was given 4 tablets of laxative (like dulcolax) to evacuate his/her colon and make examination feasible. He/she would be then asked to come for the procedure on the next morning that is day 4. If the patient had some difficulty/ reluctance with the above procedure he/she would be advised the alternate procedure. In this the patient is advised about 36 movical sachet (osmotic laxative), 9 (nine) each are used in one liter of water and consumed in 24 hours i.e. one day. These are used for four consecutive days before the procedure is due the next day. The patient was given xylocaine jelly before the start of the procedure.

However the preparatory procedure adopted for patients undergoing colonoscopy at Gastroenterology Ward of PGMI LRH was a little different and that is to give fluid diet for 2 days and give 30 ml of castor oil for 2 nights three days before the procedure and then kleen enema Bis in Die (two times a day) one day before and once in the morning just before the test. For colonoscopy in case of children, injection "Nalbin" or "Dormicum" was used to make them at ease and cooperative during

the procedure. The endoscopes used for them were also slightly different and included Olympus GIF 130, GIF 140, GIF 160 and GIF 180 type.

The sections were examined under microscope and final histopathological diagnosis was made by a Histopathologist in HMC, while representative photomicrographs of the histopathologically diagnosed disease conditions were taken at histopathology laboratory of the Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, using an advanced research microscope, Eclipse 80 I Nikon Japan.

RESULTS

General Characteristics of the patients and Groupings - A total of 90 patients with age range of 1.5 years 80 years (mean age, 27 years) were consecutively enrolled in this study. The patients were divided into two main groups on the basis of gender and then each group was further divided into five sub groups on the basis of age as depicted in (Table 1). Group-1 included patients with age less than 10 years, Group-2 included patients up to age equal to or more than 10 to 30 years, Group-3 included patients up to age more than 30 to 50 years, Group-4 included patients up to age more than 50 years while Group-5 included those patients whose age was not recorded in the ward at the time of admission/ undergoing test.

Out of the ninety (90) patients with chronic diarrhea, 48 (53.33%) had undergone endoscopic examination and 42 (46.47%) had undergone colonoscopic examination. These were further divided into male and female sub groups.

Out of the 48 cases of endoscopy only 16 (33.33%) (8 male and 8 female i.e. 50% each) showed abnormality, whereas 32 (66.67%) (22 male i.e.68.75% and 10 female i.e. 31.25%) were having grossly normal mucosa on inspection. In comparison, out of the 42 cases of colonoscopic examination 21 (50%) (9 male i.e. 42.86% and 12 female i.e. 57.14%) showed abnormality and 21 (50%) (13 male i.e. 61.91% and 8 female i.e. 38.09%) turned out to be normal on inspection.

In contrast to these results, the microscopy (histopathology) showed a different picture altogether. Eighty four out of ninety ((84/90) i.e. (93.33%) cases (50 male i.e.59.52% and 34 female i.e. 40.48%) turned out to be abnormal as compared to six out ninety (6/90) i.e. (6.67%) cases (2 male i.e.33.33% and 4 female i.e. 66.67%) which showed normal microscopic picture.

The histopathological findings on microscopy were, forty-four out of ninety (48.89%) of endoscopic biopsies that were analyzed, thirty cases (30/44; 68.18%) turned out to be of celiac disease of Marsh criteria 2a and 2b. The remaining, fourteen cases (14/44 i.e. 31.82%), were diagnosed as chronic mild non specific duodenitis and Chronic Duodenitis. Forty out of ninety cases (40/90 i.e. 44.44%) of colonoscopic biopsies that were microscopically examined twenty one (21/40 cases i.e. 52.5%) turned out to mild chronic non-specific colitis while ten biopsies (10/40 i.e. 25%) came out to be chronic active colitis and only three biopsies (3/40) i.e. 7.5% showed changes suggestive of ulcerative colitis whereas one biopsy each (1/40) i.e. 2.5% showed changes suggestive of rectal ulcer and focal active colitis. Of the remaining four cases (4/40) i.e.10%, three cases (3/40) i.e. 7.5% were polyps where as one case (1/40) i.e. 2.5% was of tubulo-villous adenoma. Only six cases i.e. 6.67% were reported microscopically as normal. Photomicrographs of representative cases of "Flatten Intestinal Mucosa C/W Celiac Disease" is shown in Figure 1, Photomicrographs of representative cases of "Tubulo-Villous Adenoma" is shown in Figure 2/

DISCUSSION

As regards to the importance and usefulness of endoscopy/colonoscopy in comparison to microscopy, scanty literature is available on these procedures in the evaluation of patients with chronic diarrhea. In this study, we evaluated (90) cases of chronic diarrhea, who underwent endoscopy/colonoscopy, for histopathological changes. We found that the grossly normal-appearing mucosa on endoscopy/ colonoscopy in majority of the cases was not actually normal on microscopic examination. In contrast to endoscopic/colonoscopic findings, only in six (6) cases (6.67%) revealed normal histology on microscopy and in the rest of eighty four (84) cases (93.33%) some degree of abnormality was observed.

These findings are clearly suggestive of the importance of performing random biopsies even in macroscopically normal appearing small intestine (duodenum, jejunum and ileum) and colon. Hence it can be deducted from this study that although both endoscopy and colonoscopy are useful but microscopy of the biopsies is relatively a more useful investigation of patients with chronic diarrhea and doing early endoscopy/colonoscopy with biopsies from both affected and normal mucosa is an important adjunctive tool for the etiological diagnosis in patients with chronic diarrhea.

No ileal biopsy/ ascending colon biopsy was taken/ received in our study. This is suggestive of either less involvement of this portion of small intestine in this

Table 1: Microscopic diagnosis of patients

Celiac disease 2a	11
Celiac disease 2b	19
Chronic mild non specific duodenitis	14
Mild chronic non-specific colitis	21
Tubulo-villous adenoma	1
Ulcerative colitis	3
Chronic active colitis	10
Polyp	3
Rectal ulcer	1
Focal active colitis	1
Normal	6

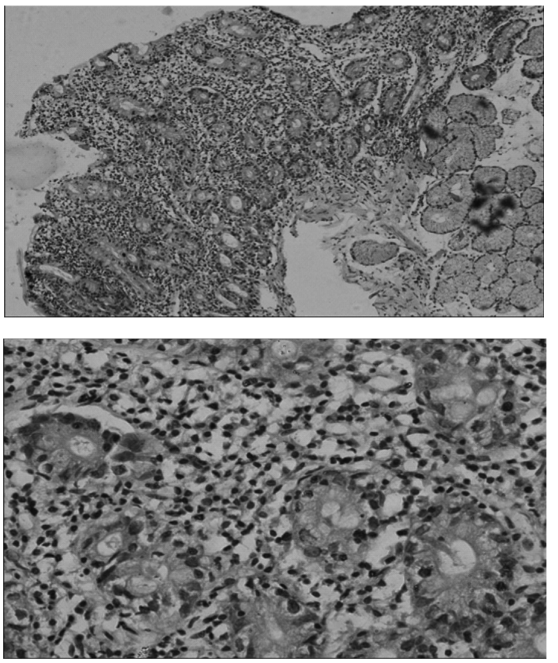

Fig. 1: Photomicrographs of representative cases of "Flatten Intestinal Mucosa C/W Celiac Disease" showing flattened intestinal villi and increased intraepithelial lymphocytes. Lamina propria contains lympho-plasmacytic infiltrate. No evidence of malignancy, granuloma or parasite is seen (H&E; A= X 100, B= X 400)

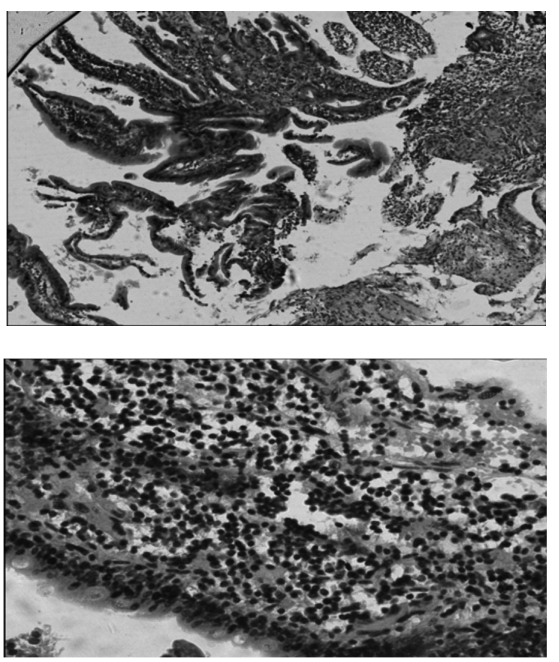

Fig. 2: Photomicrographs of representative cases of "Tubulo-Villous Adenoma" showing tubulo-papillary architecture with pseudo-stratified pleomorphic cells with prominent nucleoli. Abundant mitotic figure and lympho-plasmacyticinfiltrate is present in the background (H&E; A= X 100, B= X 400).

disease or difficulty in reaching this part by endoscopy/colonoscopy. Therefore, inflammation of ileum and ascending colon may have been missed. Thus, we cannot comment to recommend on its routine use in evaluating patients with chronic diarrhea.

Shah, et al. conducted a similar study on 228 patients. However they mainly studied colonoscopic biopsies in patients of chronic diarrhea and only two ileoscopic biopsies from ileum were also included in it. In these 228 patients 60 were excluded due to the one reason or another and out of the remaining 168 patients, 52 cases (31%) had specific histological diagnosis, 15cases (9%) had non-specific colitis and 101 cases (60%) were of normal histology.

Prior et al. studied 100 consecutive patients who were having normal colons on naked eye examination and took random biopsies from them. They found significantly low pathology i.e. only in 22% of these patients. Their slightly lower percentage of findings may be by the fact that only one-half of their patients had diarrhea.

Marshall et al., also conducted a study and wrapped up the inference that biopsies in chronic diarrhea be reserved for those patients with debilitating symptoms only. Their study group included 111 patients with chronic diarrhea who had grossly normal colons with random biopsies. However, their inference differed because they performed sigmoidoscopy alone in approximately one-third of their patients.

CONCLUSION

Early endoscopy/colonoscopy with biopsies from both affected and normal mucosa is an important adjunctive tool for the etiological diagnosis in patients with chronic diarrhea.

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