# Etiology of chronic diarrhea

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## ABSTRACT

**Objective:** The aim is to find the common causes of chronic diarrhea in our hospital, and to find out the most useful methods for diagnosis.

**Methods:** This study was carried out in the medical ward at Al-Yarmouk Teaching Hospital, Baghdad, Iraq, during the period January 1999 through to August 2000. Fifty inpatients with diarrhea for 4 weeks or more were evaluated by history, physical examination and investigations which included endoscopy with biopsy.

**Results:** The first cause of chronic diarrhea was ulcerative colitis (28%), the next was celiac disease (20%), followed equally by microscopical colitis (12%) and functional diarrhea (12%), amebiasis was the 5th cause (10%), followed by carcinoma of the colon (6%), Crohn's disease (2%), diabetic diarrhea (2%) and thyrotoxicosis (2%). Endoscopy (esophagoduodenoscopy, sigmoidoscopy and colonoscopy) with biopsy was the most useful method to diagnose >70% of the cases as ulcerative colitis, celiac disease, microscopic colitis, carcinoma of the colon and Crohn's disease.

**Conclusion:** This study revealed the importance of history taking, physical examination, and judious and sequential use of investigations especially endoscopic procedures to discover the cause of chronic diarrhea. Chronic bloody diarrhea should raise the high possibility of ulcerative colitis. A considerable number of patients with chronic diarrhea in our study were discovered to have microscopical colitis.

**Keywords:** Chronic diarrhea, etiology, hospital.

**Saudi Med J 2002; Vol. 23 (6): 675-679**

The word diarrhea originates from the Greek word (diarhein); (dia) meaning through and (rhein) meaning flow. The symptoms of diarrhea are defined as an abnormally frequent discharge form the bowel (more than 3 times per day) and a semisolid or fluid consistency of the fecal matter.[1] Diarrhea should not be defined in terms of fecal weight (for example above the upper limit of normal fecal weight (200g/d) as some persons have increase fecal weight (as high as 300g/d) but have normal stool consistency and, therefore, not complaining of diarrhea. Other persons have normal fecal weight but as their stool is loose or watery they present to doctors complaining of diarrhea. Diarrhea is termed chronic when it lasts for more than 4 weeks.[2] Each day approximately 9 liters of fluid enter the digestive tract, 2 liters represent the ingested fluid and the remainder comes from salivery, gastric, biliary and intestinal secretions that is needed to provide an appropriate milieu for food digestion. Most of this fluid is absorbed in the upper bowel, approximately one liter containing undigested dietary residue and cellular debris pass across the ileo-cecal valve to the colon.[3] The colon's principle function is to convert this liquid ileal effluent to solid feces before its advance to the rectum and is evacuated. Several important physiological processes underly normal colonic function; among these are absorption of fluid and electrolytes; peristaltic contraction that facilitate mixing, desiccation, and passage of feces to the rectum; and, finally, defecation.[4] Diarrhea can be classified on the basis of underlying mechanism. In secretary diarrhea the fecal fluid rich in sodium and potassium is lost as a consequence of impaired absorption or secretion of electrolytes by the bowel. In osmotic diarrhea, absorption of water is decreased

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Received 30th September 2001. Accepted for publication in final form 25th December 2001.

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by the osmotic effect of non-absorbable intraluminal molecules. Exudative diarrhea is caused by out pouring of necrotic mucosa, colloid, fluid and electrolytes from an inflamed colon which, in addition, is less able to carry out its normal absorptive function. An increased amount of arachidonic acid metabolites present in an inflamed mucosa may also promote increased ion secretion. Anatomic derangement of the bowel and motility disorders causes diarrhea by reducing the surface area of contact time necessary for adequate absorption to occur.[5] The incidence of chronic diarrhea in hospitalized adults ranges widely. This variation has been attributed to subjective definition of diarrhea and to the use of imprecise measurement methods.[6] Chronic diarrhea is a common symptom of many conditions, Research efforts have expanded the differential diagnosis of chronic diarrhea and have provided improved methods for the evaluation and management of patients with diarrheal disease.[7]

**Methods.** This study was conducted in the medical ward of Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from January 1999 through to August 2000. Fifty inpatients with chronic diarrhea were selected; the criteria of selection of cases were, history of diarrhea for 4 weeks or more with or without blood, mucus, tenesmus and abdominal pain. The patients with a history of diarrhea suggestive of small bowel disease, mal-odorous, large quantity and greasy stool containing food particles were included in the study. Evaluation of these patients was carried out including proper history regarding diarrhea, concerning its duration, frequency, timing (day or night), odor, consistency, amount, whether associated with abdominal pain, tenesmus, urgency, weight loss, fever and, were asked regarding any associated known illness(s) and drug(s). They were fully examined stressing mainly on general appearance, weight, presence of wasting or edema, skin pigmentation, clubbing, such as signs of malabsorption and per rectum was carried out for all cases.

A battery of investigations was carried out including general stool examination (look for red blood cells (RBCs) white blood cells (WBC) ova and parasite). Together with stool culture, blood tests including hemoglobulin (Hb), total and differential WBC, erthyrocyte sedimentation rate, blood biochemistry, liver function tests, serum iron, TIBC and calcium, for cases suspected malabsorption features, (triiodothyronine (T3), thyroxin (T4), thyrotropin (TSH)) carried out when indicated, serum protein was carried out in case of edema with malabsorption features. Radiology including chest x-ray, barium meal and follow through and barium enema when indicated. Ultrasonograghy of abdomen, upper and lower gastrointistinal endoscopy, with biopsy through the endoscope of the duodenum, rectum or colon or both, all were carried out. When ulcerative colitis (UC) is suspected endoscopically the finding were graded as follows: 1. Normal appearance mucosa. 2. Mild inflammatory changes, included absence of mucosal vascular pattern, fine granularity of the mucosa, pin point hemorrhage on mucosal swabbing and exudation of mucopus. 3. Moderate changes include coarse granularity and pin point ulceration, confluent hemorrhge. 4. Severe: gross ulceration, spontaneous hemorrhage and exudation of pus.[2] 5. In one case diabetes mellitus (DM), tests of autonomic dysfunction were carried out at bed side and the results were as follows: resting pulse rate, lying and standing blood pressure to detect orthostatic hypotension, deep breath test and hand grip test.

**Results.** The evaluation of 50 patients who fulfilled the criteria of chronic diarrhea were included in this study, 23 males (46%) and 27 females (54%), with a male to female ratio 1:1.1 and the age group ranged 10 years-70 years, and of mean age of 40 years. The final diagnosis of the selected cases and their percentage is shown in **Table 1**. The age and sex distribution of the patients and their diseases is shown in (**Table 2)**

In ulcerative colitis, there was equal male to female ratio. In Celiac disease, there was a M:F ratio of 1.5:1. In microscopical colitis, females were affected more than males. In functional diarrhea, there was an equal male to female ratio. In amaebiasis, males were affected more than females. While in carcinoma of the colon, females were

**Table 1 -** Final diagnosis number and percentage.

| **Diagnosis** | **N** | **(%)** |
|---|---|---|
| Ulcerative colitis | 14 | (28) |
| Celiac disease | 10 | (20) |
| Functional diarrhea | 6 | (12) |
| Microscopical colitis | 6 | (12) |
| Amebiasis | 5 | (10) |
| Carcinoma of colon | 3 | (6) |
| Crohn's disease | 1 | (2) |
| Diabetes mellitus | 1 | (2) |
| Hyperthyroidism | 1 | (2) |
| Undiagnosed | 3 | (6) |
| **Total** | **50** | **(100)** |
| N - number | | |

**Table 2 -** Age and sex distribution.

| Diagnosis | Sex | | Age (Year) | |
|---|---|---|---|---|
| | Male N (%) | Female N (%) | Male | Female |
| Ulcerative colitis | 7 (14) | 7 (14) | 13-65 | 21-60 |
| Celiac disease | 4 (8) | 6 (12) | 22-40 | 10-50 |
| Functional diarrhea | 3 (6) | 3 (6) | 27-42 | 32-55 |
| Microscopical colitis | 2 (4) | 4 (8) | 25-54 | 30-70 |
| Amebiasis | 3 (6) | 2 (4) | 22-49 | 30-43 |
| Carcinoma of colon | 1 (2) | 2 (4) | 38 | 55-65 |
| Crohn's disease | 1 (2) | 0 (0) | 50 | 0 |
| Diabetes mellitus | 0 (0) | 1 (2) | 0 | 43 |
| Hyperthyroidism | 0 (0) | 1 (2) | 0 | 35 |
| Undiagnosed | 2 (4) | 1 (2) | 22-64 | 68 |

N - number

**Table 3 -** Distribution of patients with chronic diarrhea according to age group.

| Age group year | N of patients |
|---|---|
| 0-9 | 0 |
| 10-19 | 6 |
| 20-29 | 10 |
| 30-39 | 13 |
| 40-49 | 11 |
| 50-59 | 6 |
| 60-69 | 3 |
| 70-79 | 1 |

N - number

**Table 4 -** Laboratory tests and their contributions to diagnoses.

| Tests | N of cases | Usefulness | N |
|---|---|---|---|
| ***Stool Examination*** | | | |
| General | 50 | +++/+ | 3/4 |
| Culture | 20 | - | |
| ***Blood*** | | | |
| Hemoglobulin | 50 | ++/+ | 1/26 |
| White blood cells | | | |
| Erythrocyte sedimentation rate | | | |
| Biochemistry (B.sugar), Urea creatinine, LFT, electrolytes) | 50 | + | 4 |
| S-iron, TIBC | 8 | + | 2 |
| S-$Ca^{++}$ | 7 | + | 3 |
| PT, PTT | 5 | + | 1 |
| S-protein | 25 | + | 11 |
| T3, T4, TSH | 2 | +++ | 1 |
| ***Radiology*** | | | |
| CXR | 26 | + | 3 |
| Barium follow through | 10 | ++/+ | 1/3 |
| Barium enema | 10 | +++/++ | 3/2 |
| Ultrasonography | 28 | ++/+ | 3/1 |
| ***Endoscopy and biopsy*** | | | |
| Upper | 19 | +++/+ | 9/3 |
| Lower | 30 | +++/++ | 27/2 |

N - number
+++ - almost diagnostic, ++ - very helpful, was contributing diagnosis with other tests, + - helpful, it narrows the spectrum of possible diagnosis,
- - not helpful
B.sugar - blood sugar,
LFT - liver function test
S.Iron - serum iron, S-$Ca^{++}$ - serum calcium
PT - prothrombin time , PTT - partial prothrombin time
S-protein - serum protein
T3 - triiodothyronine, T4 - thyroxin,TSH - thyrotropin
CXR - chest x-ray
TIBC - Total iron binding capacity

**Table 5 -** Diagnostic methods for final diagnosis

| Diagnostic method | N (%) | Case Diagnosed |
|---|---|---|
| ***Biopsy*** | 39 (74) | Celiac disease |
| Duodenal | 11 (22) | Ulcerative colitis, CA colon, |
| Rectal/colonic | 28 (56) | Crohn's disease, Microscopical colitis |
| General stool examination | 3 (6) | Amebiasis |
| Hormone estimation | 1 (2) | Hyperthyroidism |

N -number
CA - carcinoma

affected more than male. In undiagnosed cases, males were affected more than females. The distribution of the patients with chronic diarrhea according to their age group is demonstrated in **Table 3** which, showed that the most frequent incidence of chronic diarrhea was at ages 30 years to 39 years and another peak was at age group 20 years to 29 years and 40 years to 49. **Table 4** shows various diagnostic methods used with their usefulness as aids to reach diagnosis. Four grades were given to the usefulness of these tests as shown under the table. While the diagnostic methods for final diagnosis are shown in **Table 5,** in which, endoscopy with biopsy was the most common method in diagnosing cases of chronic diarrhea, followed by general stool examination, barium enema and then hormonal assessment (T3, T4, TSH).

**Discussion.** Patients with chronic diarrhea comprised a large percentage of the gastro-enterology outpatient clinic service.[7] Fifty inpatients with a history of chronic diarrhea were evaluated, regarding investigations, endoscopy (upper and lower) together with biopsy was the most useful technique diagnosing more than 70% of the patients, as is seen in other studies which showed that endoscopy was helpful in reaching the diagnosis of chronic diarrhea in more than 80% of their patients.[8] Followed by general stool examination, other investigations like blood tests (Hb, WBC count, ESR, FBS, total serum protein, liver function tests (LFT)), radiology of the intestine and ultrasonography were helpful in a lesser number of the patients. Ulcerative colitis was the first cause of chronic diarrhea (28%), the affected age ranged from 13 years-65 years, with an equal male to female ratio, the peak age of incidence in UC was 30 years-39 years. Comparing our results with the previous 2 studies carried out in our country, first by Izzat[9] who reported UC as the 4th cause of chronic diarrhea, while the 2nd study which was conducted by Shubber[10] who found UC as a cause of chronic diarrhea in 71.5% of their patients, similar observations were reported in Egypt.

Celiac disease was the 2nd cause of chronic diarrhea, (20%), with a mean age of 30 years. The peak age of incidence in celiac disease was 10 years-19 years; these findings are similar to that reported by Izzat.[9] Microscopical colitis was the 3rd cause of chronic diarrhea and the age group affected was 25 years-70 years. A group of patients (12%) who had chronic non-bloody diarrhea with a mean age of 47 years, 2:1 M:F ratio, who were classified according to histopathological features as: lymphocytic colitis in 2 patients, collagenous colitis in 2 patients and non-specific colitis in 2 patients. Microscopical colitis is increasingly diagnosed in recent last years due to our pathologists becoming more oriented in this subject and, most of the cases being diagnosed previously either as non specific colitis or functional diarrhea.[9]

Irritable Bowel Syndrome (IBS) was the 4th cause of chronic diarrhea 12%, F:M ratio 1:1. The affected age group was 27 years to 55 years, and the duration of diarrhea varies from months to 10 years. In this study we select the patients with predominant diarrhea. Izzat[9] reported functional diarrhea in 9% of their patients, but a study of 90 cases of chronic diarrhea carried out by Farfan[10] reported 20% of cases as IBS, that represent the problem in Western countries, in which functional diarrhea is much more common and estimated to be 15%-20% of the general population.[11] Our results may not reveal the true incidence of the disease, as most of these patients are treated as outpatients and rarely need admission and our study is conducted on patients admitted to the hospital.

Amebiasis was the 5th cause (10%), the affected age group was 22 years to 49 years and more common in males than females. Shubbar[10] reported in a study that (13.1%) as infective colitis including amebiasis. This lower percentage of amebic colitis in our study may be explained as most of the patients with amebiasis are treated as outpatients and they received medications including antibiotics many times which may have lead to delay and misdiagnosis of amebiasis.

Six percent of our cases had carcinoma of the colon. The affected age group was 35 years to 65 years, 2 patients were female and one patient was male. Izzat[9] found carcinoma in (6.8%) of their patients. Crohns disease was reported in one of our patients (2%). The affected age was 50 years and the main presentation was a long duration of diarrhea (1.5 years). This can be explained by the fact that their study was carried out in the gastrointestinal tract special center.

Diabetic diarrhea was diagnosed in (2%). Our patient was not responding to a diabetic diet and antibiotics and, had positive tests for autonomic dysfunction, so assumed to be due to severe uncontrolled diabetes. Diagnosis in this study depended on clinical examination and measurement of T3, T4, and TSH. Diarrhea stopped shortly after the treatment with antithyroid drugs. Six percent of our cases remained undiagnosed inspite of all the investigations. Farfan[12] reported 8.8% as undiagnosed cases. These can be explained by the following factors: 1. Our usual upper endoscopy reached only to the duodenum so we did not evaluate the 3rd part of the duodenum and jejunum endoscopically and by biopsy. 2. Lack of facilities to evaluate intestinal motility. 3. Small bowel enema (enteroclysis) is not available for evaluation of small intestine, which is far away from the reach of upper endoscopy. 4. Isolation of toxins in the stool are not carried out routinely in our hospital.[5] It is referred as chronic idiopathic diarrhea in one study,[11] and is said to be self-limiting and disappearing after a few months to a few years. The cause of this chronic idiopathic diarrhea may be idiopathic motility disturbance of bowel movement.[12] Estimations of chronic diarrhea in the absence of IBS or alternative diagnosis have ranged between 1.6 and 7.3 per 100.[11,12]

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