

Abnormalities of the Small Bowel in Chronic Infective and Non-Infective Diarrhea

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ABSTRACT

The abnormality or disease of the small intestine may cause chronic diarrhea. The tests required to investigate the abnormality of the small intestine are difficult and expensive. In this study we studied the small intestine in chronic diarrhea cases, to discover any abnormality.

The chronic diarrhea patients presenting from 1996 to 2000 (5 years) at Cipto Mangunkusumo General Central National Hospital were included in the study. Patients were excluded if unable to co-operate. All of the patients were given blood and stool tests in addition to colonoscopy, ileoscopy and duodeno-jejunoscopy with biopsy.

Small intestinal examination could only be performed on 78 patients with chronic diarrhea. The most frequent characteristic were: aged 30-39 or 50-59 years (25.6% of all cases in the study), male (57.7%), non-bloody non steatorrheic type of diarrhea (74.4%), and 4 to 48 weeks duration of diarrhea (68.0%). Small intestine abnormalities were endoscopically and/or histopathologically found in 65 cases (82.6%), while the rest of the patients were found to have normal small intestine. The abnormalities were found to be infective non-tuberculosis ileitis (in 20 patients, or 26% of all cases), Infective non-tuberculosis duodenitis (20,

or 26%), non-infective jejunitis (14, or 18.2%), villous atrophy of the jejunum (3, or 3.9%), lymphoid nodular/follicle hyperplasia of the terminal ileum (12, or 15.6%) etc. Large intestinal abnormalities were found in 67 or 85.7% of the chronic diarrhea cases.

The frequent small intestinal abnormalities were infective ileitis, duodenitis and lymphoid nodular/follicle hyperplasia of the terminal ileum. The small intestinal abnormalities were found less than the large intestinal abnormalities.

Keywords: Small Intestine, Chronic Diarrhea, Histopathology, Lymphoid Follicle Hyperplasia

INTRODUCTION

Any abnormality or disease of the small intestine may cause chronic diarrhea.^{1,2,3} Chronic diarrhea is very commonly found in Indonesia.^{4,5,6,7} The tests required to investigate any abnormality of the small intestine are difficult and expensive.^{8,9,10} The causes of chronic diarrhea in the small intestine can be divided as infective and non-infective or functional and organic.^{8,9,10} In developing countries the most frequent cause of chronic diarrhea is infection.^{5,10,11,12,13} The bacterial causes of infective diarrhea are pathogenic *E.coli*, *Shigella spp*, *Salmonella spp*, *Yersinia spp*, *Clostridia spp*, *Mycobacterium tuberculosis*. Parasitic causes of infective diarrhea are *Giardia lamblia*, *Cryptosporidium parvum*, *Isospora belli*, *Microsporidia*, *Strongyloides stercoralis*. Fungal cause of infective diarrhea are *Candida albicans* and *histoplasmosis*.³ The non-infective causes of chronic diarrhea in the small bowel are ischemic enteritis, Crohn's disease, NSAID enteropathy, radiation enteropathy, eosinophilic enteritis, irritable bowel syndrome (IBS).³

The objective of this study was to describe the abnormalities of the small bowel and the (potential) causes of chronic infective and non-infective diarrhea in Indonesia.

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MATERIALS AND METHODS

We examined all chronic infective and non infective diarrhea patients between 1996 and 2000 who underwent small bowel tests (both endoscopic and histopathological). The patients included in this study were from Division of Gastroenterology, The Department of Internal Medicine, Cipto Mangunkusumo General Central National Hospital, Jakarta, Indonesia. Each of the patients received physical examination, stool tests, a peripheral blood test, a liver function test, a pancreatic test (serum amylase-lipase), if necessary a thyroid function test. We excluded patients who were unable to cooperate. Gastroduodenojejunoscopy and ileocolonoscopy were performed on each case. If deemed necessary, a small bowel x-ray with double contrast was also performed to determine any small bowel disorder. The economical status was classified into good-average and bad class according to the history of the patients welfare and ability to buy food/medicine etc.

We took 2 biopsy specimens from the duodenal bulb, 2 specimens from the pars descendens duodenum, 2 specimens from the jejunum near the ligamentum Treitz, 2 specimens from the terminal ileum and 4 specimens from the colon for histopathological tests. We used a small calibre pediatric colonoscope-an Olympus PCF-10 for the gastroduodenojejunoscopy. We used an Olympus CF-200 for the ileo-colonoscopy. The specimens were processed and examined in the Department of Pathology Anatomy University of Indonesia and the results were later checked at the Academic Medical Centrum, University of Amsterdam. The histopathological specimens were stained with Haematoxyllin-Eosin.

Chronic diarrhea was diagnosed if the passage of stool was more than 200g per day or if passage of soft and watery stool was more than 3 times per day with or without blood or mucous in the stool and it lasted more than 15 days.^{4,6,14,15,16,17,18} Diarrhea was diagnosed as infective if a (potential) pathogenic microorganism was isolated. The case would be diagnosed as non-infective diarrhea if such microorganisms were not observed.^{19,20} Candida would be considered as a possible cause of chronic diarrhea if stool direct examination for Candida (hyphae/spore) turned out to be positive or if a large amount of Candida growth was discovered in the stool culture (++ or +++ or more than 10 colonies in culture or more than 10.000 colonies in 1 g of stool) or if characteristic candidiasis was seen on colonoscopy/ileoscopy examination.^{21,22} The Criteria: + if there were only a few colonies, less than 10 colonies, on stool culture. ++ if

there were a lot of candida colonies on stool's culture, more than 10 colonies. +++ if we could find candida on direct stool examination with microscope or there were too many candida colonies on stool culture, difficult counting due to too much candida colonies. Candida were thought to be only intestinal commensal if candida in stool culture was found only + and there was no improvement after anticandida therapy. Negative infection of Candida if we found no candida in direct examination or found only a few colonies of candida (less than 10 colonies or less than 10.000 colonies in 1 g of stool) in culture examination. *Blastocystis hominis* would be considered as a possible cause if we found a large amount of *Blastocystis* in direct examination of the stool (++ or +++) and no other causes were found.^{23,24} Carbohydrate maldigestion was considered if we found abundant amyllum or undigested carbohydrate in the stool. Fat maldigestion was considered if abundant fat was found in the stool by qualitative examination with Sudan staining.

The data were analyzed with chi-square or fisher test.

RESULTS

We have performed small intestinal examinations (duodeno-jejunoscopy and ileoscopy) on 78 patients during a five-year period (1996-2000). The most frequent characteristics of the patients were of the 30-39 or 50-59 years old (25.6%), were male patients (57.7%), most had a good socioeconomic status (98.7%), and they had non-bloody non steatorrheic type of diarrhea (74.4%), with a duration of diarrhea >48 weeks (68.0%) (table 1). There were no significant differences on the characteristics between the infective diarrhea and non-infective diarrhea ($p > 0.05$).

The laboratory results of the patients can be seen in table 2. There were no significant differences on the laboratory results between the infective diarrhea and non-infective diarrhea ($p > 0.05$).

Through endoscopic and/or histopathological examinations, small intestine abnormalities were found in 83.3% of all cases, and the rest of the patients were found to have normal small intestines (see table 4, figure 1 and 2). Large intestinal abnormalities were found in 67 or 85.7% of the chronic diarrhea cases (table 5).

In the duodenal bulb, the characteristic of patients (age, sex, and duration of diarrhea) were not correlated with the endoscopic abnormalities ($p > 0.05$, not significant). In the jejunum and terminal ileum, the age was correlated with the endoscopic abnormalities ($p < 0.05$), but the sex and duration were not correlated with the

Table 1. The Characteristics of The Chronic Diarrhea Patients

Characteristics	Total Patients Frequency(%)
Age Group:	
10 - 19	2(2.6)
20 - 29	16(20.5)
30 - 39	20(25.6)
40 - 49	8(10.3)
50 - 59	20(25.6)
60 - 69	10(12.8)
70 - 79	2(2.6)
Sex: Male/Female	45/33(57.7/42.2)
Economical Status:	
Good-average	77(98.7)
Bad	1(1.3)
Stool form of diarrhea:	
Bloody	18(23.1)
Steatorrhea	2(2.6)
Non-bloody non-steatorrhea	58(74.4)
Frequency of diarrhea per day:	
4-10 x	75(96.2)
> 10 x	3(3.8)
Duration of diarrhea (weeks):	
3-4	15(19.2)
> 4-48	53(68.0)
> 48	10(12.8)

Table 2. Laboratory Results

Laboratory Examinations	Infective (frequency)	Non-Infective (frequency)	p- value	Total Patients Frequency(%)
Hemoglobin (g%):				
< 12	9	3	NS	12/51(24)
≥ 12	27	12		39/51(76)
Albumin (g/dl):				
< 3.5	3	2	NS	5/25(20)
≥ 3.5	16	4		20/25(80)
Leucocyte(/mm ³):				
< 5000	5	2	NS	7/47(14.7)
5000 - 10000	22	11		32/47(68.3)
> 10000	7	1		8/47(17.0)
Stool leucocyte(/field):				
0	12	4	NS	16/40(40)
≥ 1	20	4		24/40(60)
Stool erythrocyte(/field):				
0	20	6	NS	26/41(63.4)
≥ 1	13	2		15/41(36.6)
Maldigestion(stool exam.):				
- Negative	21	12	NS	33/72(45.8)
- Carbohydrate	26	7		33/72(45.8)
- Fat	1	0		1/72(1.4)
- Carbohydrate and fat	4	1		5/72(6.9)

Note: NS=not significant

Table 3. Stool Examination on Bacteria, Parasite and Fungus in Patients with Infective Diarrhea

Stool Examination	Frequency	Percent
Bacterial culture:		
Alcaligenes dispar	3	3.9
Clostridium perfringens	1	1.3
Pathogenic E.Coli	17	22.1
Salmonella paratyphi	2	2.6
Klebsiella ozaenae	3	3.9
Klebsiella pneumonia	3	3.9
Klebsiella oxytoca	4	5.2
Enterobacter aerogenes	2	2.6
Shigella flexneri	1	1.3
Aerobacter aerogenes	1	1.3
Tuberculosis	1	1.3
Negative/normal flora	34	44.2
Parasite:		
Blastocystis hominis	1	2.9
Giardia lamblia	1	2.9
Candida albicans	26	76.4
Entamoeba histolytica	1	2.9
Ankylostoma duodenale	1	2.9
Trichuris trichiura	4	5.9

Note: 1 patient could have one or more pathogens

Table 4. Result of Endoscopic and Histopathologic Examinations of the Small Intestine in 78 Patients with Chronic Diarrhea

Results	Frequency	Percentage
Small intestinal abnormalities:		
Yes	65	83.3
No	13	16.7
Duodenum:		
Infective non TBC duodenitis	10	13.0
Non-infective duodenitis	20	26.0
Duodenitis + villous atrophy + giardiasis	2	2.6
Duodenitis + lymphoid follicle hyperplasia	2	2.6
Normal	44	56.4
Jejunum:		
Villous atrophy due to Celiac disease	1	1.3
Villous atrophy due to Giardiasis	2	2.6
Infective jejunitis	9	11.7
Non-infective jejunitis	14	18.2
Infective jejunitis + Lymphoid follicle hyperplasia	1	1.3
Non-infective jejunitis + Lymphoid follicle hyperplasia	1	1.3
Normal	50	65.0
Ileum:		
TBC	6	7.8
Infective(nonTBC) ileitis	20	26.0
Crohn's disease	4	5.2
Non-infective ileitis	5	6.5
Lymphoid follicle hyperplasia	1	1.3
Infective(nonTBC) ileitis + Lymphoid follicle hyperplasia	8	10.4
Non-infective ileitis + Lymphoid follicle hyperplasia	3	3.9
Normal	30	39.0

Table 5. Result of Endoscopic and Histopathologic Examinations of the Colon in 78 Patients with Chronic Diarrhea

Results	Frequency	Percentage
Infective non TBC	44	56.4
Infective + Lymphoid follicle hyperplasia	3	3.9
TBC caecum	4	5.2
Trichuriasis	1	1.0
Ulcerative colitis	4	5.2
Crohn's disease	4	5.2
Non infective colitis	4	5.2
Malignant lymphoma	1	1.3
Polyp	2	2.6
Normal	11	14.3

endoscopic abnormalities ($p > 0.05$, not significant).

The histopathologic differences between infective and non-infective diarrhea are shown in table 6.

DISCUSSION

During the five-year period between 1996 and 2000, we performed small intestine examinations in 78 chronic diarrhea patients. This rather low number was caused by the uncooperative patients, incomplete data as well as other reasons.

Age between 30-39 years or 50-59 years was the most frequent characteristic of the patient; this was different if compared to the results of other studies.^{5,25,26}

Most patients were males, and this supported the results of previous studies.^{5,26} Other findings have also shown that males often eat outside their homes, the food is usually not hygienic, causing them to suffer more chronic diarrhea. We know that conditions hygiene in Indonesia is still far from ideal.

The most frequent stool form was nonbloody-nonsteatorrhea. This confirmed the results of other studies.⁵ The most frequent length of the chronic diarrhea was from >4 to 48 weeks. This result was varied compared to other studies, one study reported that the average duration of chronic diarrhea was 45.7 ± 52.4 months (1-240 months).^{5,26}

Small intestinal abnormalities were found in 82.6% of the chronic diarrhea patients endoscopically and histopathologically, and large intestinal abnormalities were found in 85.7% of the patients. These findings were the same as in the literature which stated that the most frequent abnormalities in chronic diarrhea were in the colon.^{8,10}

In the western countries, celiac disease is one of the frequent causes of malabsorption in the gastrointestinal tract. The usefulness of the biopsy has already been established, and it is considered the most important diagnostic tool for diagnosing malabsorption.^{1,2,3} In this study we found three cases of villous atrophy due to giardiasis or celiac disease, which could cause malabsorption, malnutrition and chronic diarrhea.

The frequent abnormality in this study was infection, this finding was in line with other reports in developing countries. According to existing literature^{8,10,11,12,13}, frequent causes of bacterial infections include pathogenic E.coli, Salmonellosis, Shigellosis etc. Frequent parasite infection of the gastrointestinal was Giardia lamblia.

Table 6. Histopathologic Appearances in Infective and Non-infective Diarrhea

Small bowel	Infective	Non-infective	p-value
Duodenum:			
Intraepithelial lymphocyte:			
+	52	23	Ns
++	1	0	
+++	1	1	
Lymphocyte: +	43	21	Ns
++	11	2	
Plasma cell: +	45	23	Ns
++	9	1	
Polymorphonuclear cell: 0	19	20	0.001
+	28	4	
++	7	0	
Jejunum:			
Intraepithelial lymphocyte:			
+	51	23	Ns
++	2	0	
+++	1	1	
Lymphocyte: +	44	22	Ns
++	10	2	
Plasma cell: 0	1	0	Ns
+	48	23	
++	5	1	
Polymorphonuclear cell: 0	23	19	<0.01
+	25	5	
++	6	0	
Terminal Ileum:			
Intraepithelial lymphocyte:			
+	51	23	Ns
++	2	1	
+++	1	0	
Lymphocyte: +	30	21	0.013
++	24	3	
Plasma cell: +	28	20	0.017
++	26	4	
Polymorphonuclear cell: +	11	23	<0.001
++	24	1	
+++	19	0	

The lymphoid follicle/nodular hyperplasia in the terminal ileum(15.6%) which was found in 15.6% of cases, could have been caused by infection, inflammation or normal variation.

We could not determine whether the small intestine or the large intestine had the dominant role in causing chronic diarrhea. In this study we just studied the abnormalities in small intestine in chronic diarrhea cases.

Histopathologically, there were more polymorphonuclear cells infiltration in the infective group compared

to the non-infective group. This finding is inline with other studies about infective small bowel or infective colitis.^{27,28}

CONCLUSION

The abnormalities most frequently found in the small intestine were infective ileitis, duodenitis and lymphoid nodular/follicle hyperplasia of the terminal ileum. The small intestinal abnormalities were found less than the large intestinal abnormalities.

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