

SPECIAL ARTICLE

Persistent Diarrhea : Possible Risk Factors in Indonesia

by

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Abstract

From the management point of view, acute diarrhea in Indonesian children is not a big problem anymore. Persistent diarrhea, although the prevalence is less than 10% of acute diarrhea, but the case fatality rate is about 5-7 times higher which is account for 30-50% of total diarrhea deaths.

*There are many factors which may contribute to the etiologies of persistent diarrheas. They are among others the specific agents mainly the invasive bacterias (*Galmonella spp*, *Shigella spp*, *Campylobacter spp*, *Enteroinvasive E.coli*, etc.), *Giardia lamblia* and *E.histolytica*; malnutrition, malabsorption syndromes, systemic infections mainly measles; and last but not least the missmanagement of acute diarrhea, particularly the abundance use of antibiotics and antidiarrheal agents, the late of giving food to the patients and the too early giving semisolid food in normal young baby less than 4-6 month of age.*

Introduction

Most of acute diarrhea episodes are lasting less than 5 days. In most places, only 1/4 - 1/5 of cases last longer than 7 days and only some 5 - 15 % last longer than 14 days. Acute episodes of diarrhea which are thought to be caused by infection and which last 14 days or longer are defined as persistent diarrhea. Chronic diarrhea is a broad category of diarrhoea conditions including long-standing illnesses of non-infectious etiology, such as tropical sprue, gluten sensitive enteropathy or celiac disease and hereditary diarrheal disorders. So, in general it could be separated into 2 different entities : chronic diarrhea of non-infectious origin and

persistent diarrhoea of infectious origin [1].

These few cases of persistent diarrhea are very important, due to the following reasons : (1) they account for 45 - 50 % of total diarrheal days; (2) they have a risk of growth faltering or weight loss 3 times greater than episodes lasting less than 7 days; (3) they have a high risk of death, up to 5 - 7 times higher compared to acute diarrhea; (4) they account for 30 - 50 % of total diarrhea deaths.

Because of these factors, persistent diarrhea are often brought to doctors and occupy a large percentage of diarrhoea beds in hospitals.

Prevalence

The prevalence of persistent diarrhea in Indonesia is still unknown. It is thought to vary from place to place and region to region. The differences in urban and rural areas are very likely as breast feeding practices are still normal in rural areas. Munir (1982) reported the prevalence of 4 % among 1184 hospitalized diarrheal cases in Manado, North Sulawesi, from 1977-1980 [2]. In the second survey, from 1980-1983, it was found that 25.3 % of 391 hospitalized diarrhea patients had diarrhea lasting more than 7 days and 4,3 % more than 14 days. Suharyono (1985) in Jakarta found that 5.0 % out of 1014 acute diarrheal patients below 2 years of age became persistent [3]. These figures

could be reduced up to 2.16 % only one year later [4].

Regarding the age incidence, it was reported by Munir (1982) in the first study that the ages ranged from 2 to 41 months, 66 % of them were infants below 1 year of age, whereas in the second study the age ranged were 1-35 months [2]. Soeparto et al. (1982) in Surabaya, East Java, reported the percentage of 89 % in children below 18 months of age [5].

Sutanto (1982) from Medan, North Sumatera, reported a percentage of 76.2 % in children below 1 year of age in the study among 576 ambulatory patients with PEM and diarrhea, and 15.9 % of them had persistent diarrhea [6].

Causes and Risk factors

A great number of factors may contribute to the mechanism of persistent diarrhea. They are, among others, ignorance, taboo beliefs and behaviours, hot and humid climate, low purchasing power, poor housing conditions, inadequate clean water supply, lack of personal hygiene, improper environmental sanitation, high incidence of malnutrition, high incidence of infections and infestations, overcrowding family, many children under 5 years of age in one household, food allergy, food intolerance particularly lactose intolerance, fat malabsorption and protein intolerance, etc.

It is very difficult to determine a single cause of etiology among these multi-complex factors. The most important pre-disposing factors in Indonesia may be: (1). poor environmental sanitation and personal hygiene; (2). prevalence of malnutrition and infection, and (3). malabsorption syndromes.

From the clinical epidemiological point of view, causes of persistent diarrhea may be grouped into: (1). specific infectious agent, (2). host factors, and (3). other factors.

1. Specific Infectious Agent

Most of enteropathogens that cause acute diarrhea, with the exceptions of *V.cholera* and viruses (particularly *Rotavirus*) may have also been associated with persistent diarrhea. The enteropathogens which may cause persistent diarrhea can be divided into 2 broad groups, i.e.:

- a. Those that are isolated with greater frequency from episodes of persistent diarrhea, e.g. *Enteroadherent E.coli* (EAEC), *Enteropathogenic E.coli* (EPEC) and *Cryptosporidium*.
- b. Those that are isolated in equal frequency from episodes of persistent and acute diarrhoea, e.g. *Shigella*, non typhoid *Salmonella*, *Campylobacter*

jejuni, *Enteropathogenic E.coli* (EPEC), *Giardia lamblia*, and *Entamoeba histolytica*.

The tendency for certain organisms to cause longer-lasting diarrhea maybe related to the capacity of the organism to adhere to or invade the bowel mucosa. A severe acute episode may have greater tendency to cause persistent than non severe episodes.

Soeparto et al. found that the most common enteropathogens isolated were *E.coli* (32.1 %) followed by *Salmonella spp* (17.9 %) and *Staphylococcus aureus* (10.7 %). Protozoal infections, such as *Entamoeba histolytica* and *Giardia lamblia* may cause persistent diarrhea too [5]. In a separate study, Soeparto found that half of the children with amebiasis investigated experienced diarrhea for more than 2 weeks. Giardiasis is generally accepted as cause of persistent diarrhea, fat malabsorption and malnutrition. Eight of 30 infants with malnutrition showing positive giardiasis in their duodenal aspirates were also suffering from persistent diarrhea [6].

2. Host Factors

a. Malnutrition

Diarrhea in malnourished children always lasts longer and is more likely to become persistent. Experience in animal diarrhea models indicates that this is because malnutrition impairs the ability of the gut epithelium to replace damaged cells and restore normal enzymes and absorptive function. Compared with controls, malnourished rats reduced the small intestinal weight, length and diameters, small intestinal mucosal weight and specific enzyme activities of lactase, sucrase and maltase [7]. Additional mechanism is immunologic suppression in malnourished

children and in children during and after measles. With the impaired immunological function, children are unable to eliminate the causative organisms, which thus persist damaging mucosal cells.

Studies on the serum and small intestinal immunoglobulin levels in undernourished children with diarrhea revealed equality elevated levels of intestinal immunoglobulins. Intestinal infections appeared to elevate IgG levels more than secretory IgA levels in the age group examined. However, it appeared likely that the IgG was serum derived, whereas the IgA appeared to be locally produced. There was no apparent deficiency in the capacity of undernourished children to manufacture and secrete immunoglobulin in the gut [8].

Studies on the immunological contents of breastmilk in Indonesian children revealed that the protein content and the antibodies level against *E.coli*, *Staphylococcus spp* and *Salmonella spp* were almost similar as in the breastmilk of Australian mothers, with a somewhat lower content of immunoglobulin and lactoferrin in the breastmilk of Indonesian mothers [9]. These lower content of immunoglobulin and lactoferrin might be related to the nutritional state of the mothers. Household survey in 1980 and 1985 revealed that 70 % of the pregnant women were anemic.

b. Carbohydrate malabsorption

Deficiencies of digestive enzymes particularly lactase and sucrase may result in persistent diarrhea. Sunoto et al. in Jakarta found that 40 % out of 50 children with persistent diarrhea were associated with lactose intolerance [10]. Munir in Manado [2] and Soeparto et al [5]. in Surabaya found only 4.0 % and 5 % respectively. These discrepancies are thought to be due to differing severity of the disease, accompanying diseases such as malnutrition and the methodology used. Sunoto et al. for example found a per-

centage of 86.4 % of lactose intolerance in the study of severe malnutrition by using lactose loading test method [11]. Such deficiencies are usually caused by infectious diarrhea, whereas host factors such as malnutrition influence the degree of the deficiency and the time needed for recovery. Administration of foods containing large amounts of food substance which cannot be digested (e.g. undiluted milk containing lactose) may lead to malabsorption of the administered food or fluids and a persistent osmotic diarrhea.

c. Fat malabsorption

Fat malabsorption can be investigated by using macroscopic stool examination which indicates the presence of fat globule, Rossipal's floating test [12], Lipiodol absorption test and steatocrit test [3]. The percentage of fat malabsorption, in fact, is higher than lactose intolerance. Boediarso et al. found steatorrhea in 62.5 % of 831 infants, consisting of 89.5 % of 76 low birth weight infants, 60.9 % of 121 fullterm neonates and 57.9 % of 331 infants with diarrhea and malnutrition [13]. Soeparto et al. found a percentage of 41.7 % among children with diarrhea and malnutrition [5].

The nasional household survey in 1972 and 1980 revealed that the incidence of LBW infants among newborn babies were 20 % and 14 % respectively. The incidence of malnutrition among underfives in 1980 was 30 %, 12 % of them in the severe form, which 5 years later could be reduced to 12 %, 1.2 % of them in the severe form 5 years later.

d. Protein intolerance

Protein intolerance or cow's milk protein sensitive enteropathy (CMPSE) may cause persistent diarrhea. Soeparto et al. in Surabaya found that 72.9 % of persistent diarrhea were due to CMPSE [14]. The

high incidence of CMPSE is said to be attributed to the declining tendency of mothers breastfeeding their babies. The presence of CMPSE also has been reported by Sutjningsih et al. (1980) and Munir et al. (1982) [2,15].

e. Small bowel villous atrophy

Small bowel biopsy in Indonesia was first performed by Suharyono et al. on severe malnourished children with diarrhea in Jakarta [16]. Several grades atrophy of the small intestinal mucosa was found in almost all patients. The more severe the degree of malnutrition the more severe the atrophy and the longer the diarrhea. Grade IV, V, and VI atrophy were found in 56.3 % of the patients, whereas the rest were in grade II and III atrophy. Soeparto et al. performed intestinal biopsy in 33 patients with chronic diarrhea and severe malnutrition. The results of the biopsy revealed that in 15.1 % of the patients had grade IV abnormalities, whereas the rest were still in grade I and II [14].

f. Infection and infestation

1. Bacterial infection

Stool culture for bacteriological examination in 84 children with prolonged diarrhea (diarrhea lasting for more than 7 days) revealed that 53.6 % excreted enteropathogen. The most common was *E.coli* as much as 32.1% [5]. Munir et al. in Manado found microorganisms from the stool in 41.2 % of the patients [2]. Gracey et al. found a marked microbial contamination of the upper gastrointestinal tract with a wide variety microorganisms in 21 children with malnutrition and diarrhea [17]. Significant overgrowth of anaerobes were isolated. Overgrowth of anaerob bacteria in the gastrointestinal tract produce a wide range of clinical effects including steatorrhea, carbohydrate malabsorption, hypo-

proteinemia, vitamin B12 deficiency and it is associated with microcytic anemia and iron deficiency.

2. Intestinal parasitic infection

Giardia lamblia, *Entameba histolytica*, *Cryptosporidium* are the main causes of persistent diarrhea. The prevalence of giardiasis in Indonesia shows great variation (Sunoto, 1980). Soeparto et al. [5] in Surabaya found a prevalence of 18 % giardiasis in 28 children (0-2 years) with persistent diarrhea, whereas Sahetapy et al. found a prevalence of 27 % [18].

Amebic dysentery was found in 19 % of the children with persistent diarrhea in Medan [6], whereas in Yogyakarta it was found in 39.0% [19]. Of these cases, 68.7 % revealed fat malabsorption by using lipiodol absorption test (LAT).

Several investigations regarding intestinal candidiasis in children with malnutrition and diarrhea have been done [20]. Studying the duodenal and gastric content of 21 malnourished children with diarrhea revealed significant growth of *Candida* spp. In 8 (40 %) of the patients the number of isolation were more than 10000 colonies per milliliter fluid [17]. Studies on the candida-killing ability of polymorph in 67 wellnourished and malnourished children revealed that malnourished children had an impaired candidacidal activity of leucocytes. In wellnourished children the mean candidacidal activity was 44.5 %, whereas in severe malnourished children it was 13.7 % [21].

3. Accompanying diseases (parenteral infection).

Accompanying systemic infections, such as measles, pneumonia, septicemia, etc., may play a role in causing acute diarrhea to become persistent [22]. Measles may cause damage of the intestinal mucosa

thus causing protein losing enteropathy. Pneumonia and septicemia may cause high fever which could disturb the activity of the intestinal enzymes and decrease the immune response, thus decreasing the control of the enteropathogenic bacteria in the small intestine.

3. Other Factors

A previous episode of persistent diarrhea, or a recent episode of acute diarrhea, ap-

pear to increase the risk of persistent diarrhea of unknown mechanism. Ineffective management of acute diarrhea has been thought to contribute to the development of persistent diarrhea. Delay in restarting breastfeeding or feeding, the use of antimotility drugs for acute watery diarrhea, all have been postulated as causative factors. Further studies are required to determine if these or other diarrhea managerial practices are risk factors for persistent diarrhea.

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