PATHOGENS DIARRHEA IN CHILDREN, RISKS AND TREATMENT

By

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Abstract

Diarrhea is the condition of having at least three (or more than in normal individual), loose, liquid, or watery bowel movements each day, or for few days resulting in dehydration due to fluid loss. Signs of dehydration often begin with loss of the normal stretchiness of the skin and irritable behavior by decreased urination, loss of skin color, a fast heart rate, and a decrease in responsiveness as it becomes more severe. Loose but non-watery stools in babies who are exclusively breastfed, however, are normal. Frequent passing of formed stools is neither diarrhea, nor is the passing of loose, "pasty" stools by breastfed babies.

Diarrhea is usually a symptom of an infection in intestinal tract caused by many bacterial, viral and parasitic organisms. Infection is spread through contaminated food or water, or from person-to-person as a result of poor hygiene.

Keywords: Diarrhea, Children, Youth, Adults, Bacteria, Virus, Overview

Introduction

Diarrhea is defined as passage of three or more loose or liquid stools per day (or more frequent passage than is normal individual). Frequent passing of formed stools is not diarrhea, nor is the passing of loose, "pasty" stools by breastfed babies, defined as the passage of three or more loose or watery stools per day (WHO, 2017). Nevertheless, absolute limits of normalcy are difficult to define; any deviation from the child's usual pattern should arouse some concern (especially with ill appearance, passage of blood or mucus, or dehydration) regardless of the actual number of stools or their water content.

Diarrhea could be: 1- Acute diarrhea (including cholera), 2- Persistent diarrhea for 2 weeks or more, 3- Severe persistent diarrhea or persistent diarrhea with some or severe dehydration), and 4- Bloody diarrhea or dysentery blood in the stool (King et al, 2003).

Review and General Discussion

Acute infectious gastroenteritis by viruses totals for most bouts of diarrhea in resource-rich countries, resulted in more than 1.5 million outpatient visits and 200,000 hospitalized in the USA annually (Cohen, 1991).

Life-threatening conditions: Many disorders may cause life threatening diarrhea may be in children (Algorithm 1A), mainly urgent are intussusception, hemolytic uremic syndrome (HUS), pseudomembranous colitis, appendicitis, toxic megacolon, and in very young infants, congenital secretory diarrheas (Pereira and Hsu, 2016).

Intussusception: Intussusception refers to invagination (telescoping) of a part of the intestine into itself, with most common abdominal emergency in early childhood, particularly in children younger than two years of age (Lloyd and Kenny, 2004). Intussusception is most common from 6 to 12 months of age, and the vast majority of cases occur in the first two years of life. Most children with intussusception develop the sudden onset of intermittent, severe, cramp abdominal pain, accompanied by inconsolable crying and drawing up of legs toward the abdomen, but some present with bloody diarrhea. The episodes of pain usually occur at 15 to 20 minute intervals. They become more frequent and may be followed initially by emesis of gastric contents. Bilious emesis may develop as obstruction progresses. Between the painful episodes, the child may behave normally. As a result, initial symptoms can be confused with gastroenteritis. As symptoms progress, increasing lethargy develops that can be mistaken for meningitis (Fleisher, 2010).

Attacks also can be separated by periods of apathy followed by vomiting and the passage of currant jelly stool as a mixture of bl-
ood and mucus, and a sausage-shaped abdominal mass felt in right abdominal side (Yamamoto et al, 1997). Prevalence of blood in stool was up to 70%, if occult blood was included and increased with symptoms duration. But, classically described triad of pain, a palpable sausage-shaped abdominal mass, and currant-jelly stool is seen in <15% of patients at the presentation time. Up to 20% of young infants have no obvious pain. Patients don’t pass blood or mucus or develop an abdominal mass in about 30% of cases. Some infants and many older children have pain without other signs or symptoms (Cera, 2008).

Intussusception is a common cause of bowel obstruction in young children with significant morbidity and mortality if not promptly treated (Ntoulia et al, 2016). Intussusception is unusual in adults, and the diagnosis is commonly overlooked. In the majority of adults, a pathologic cause was identified (Erkan et al, 2005). Intussusception was typically seen in 6 to 36 months of age, as the commonest cause of intestinal obstruction in this age group. About 60% of children with intussusception was < a year old, & 80 to 90% were < two years (Mandeville et al, 2012). Buettcher et al. (2007) in Switzerland on population-wide survey reported that yearly mean incidence of intussusception was 38, 31, & 26 cases/100,000 live births in first, second, and third year of life, respectively, but after the third year, rates dropped to < 0.5. Yap Shiyi and Ganapathy (2017) in Singapore reported that intussusception is usually diagnosed in younger population <1 year predominantly males. They found that older Asian children can also have intussusception. The classical triad was not a very sensitive diagnostic tool, but combination of abdominal pain, in drawing of legs, and vomiting may be a more common presenting triad in them. Park and Cho (2021) in South Korea concluded that clinical findings of ileocolic intussusception varied due to age and symptoms’ duration. Younger children with paroxysmal pain, vomiting, bloody stool, poor oral intake, or lethargy must be suspected having intussusception, but older ones, non-specific abdominal pain without bloody stool was a symptom of intussusception, and contrast enema helped to diagnose intussusception in them without typical symptoms. Kaiser et al. (2007) reported that success of intussusception reduction was improved by air-contrasted techniques, not affected by previously failed attempts, and that delay diagnosis decreased radiologic reduction and increased risk of operative intervention of bowel resection. Zhang et al. (2015) found that intussusception was not usually immediately life-threatening. But, successful treated with barium, water-soluble, or an air-contrast enema, which confirmed diagnosis and successfully reduced it. Success rate was > 80%, but up to 10% may reoccur within a day.

Hemolytic uremic syndrome: Hemolytic uremic syndrome (HUS), although uncommon, merits consideration in any child with bloody diarrhea, particularly in the first five years of life, as a potential fatal illness (Gasser et al, 1955). It complicates 6 to 9% of entero-hemorrhagic E. coli O157:H7 strain infections and started 5 to 10 days after diarrhea onset, HUS with a sudden onset characterized by triad of: 1- Micro-angiopathic hemolytic anemia, 2- Thrombocytopenia, & 3- Acute renal failure (Noris and Remuzzi, 2005). The E. coli O157:H7 infectious dose for man was 10 to 100 organisms which was low compared to other enteric pathogenic ones (Lim et al, 2010): Shigella: 10 to 100, Campylobacter jejuni: 10(4) to 10(6), Salmonella: 10(5) to 10(8), enterotoxigenic E. coli: 10(8), Vibrio cholera: 10(5) to 10(8), & Yersinia enterocolitica: 10(9). Cattles are the E. coli O157:H7 natural reservoir, from 1% to 50% of healthy ones carry & shed E. coli in their feces at any time and contaminated ground beef is the commonest vehicle for E. coli O157:H7 outbreaks (Dunn et al, 2004).

Children typically have a prodromal illness with abdominal pain, vomiting, and diarrhea that precedes the development of HUS by a few days, as a result of which a patient
may not have signs of hemolysis or renal failure when seen earlier stage. Diarrhea associated with gastrointestinal complaints may mimic those of ulcerative colitis, other enteric infections, and appendicitis. Clinical features after 3-8 days incubation, with first symptom was watery diarrhea, followed by bloody diarrhea and abdominal cramps, nausea and vomiting, but fever less commonly seen (Ahn et al, 2008). The most important factors associated with HUS evolution are the use of anti-motility agents, antibiotics, bloody diarrhea, leukocytosis, young age & females. Risk of developing HUS after bloody diarrhea due to E. coli in about 15%, but with spontaneous recovery, and 26% of the patients developed renal failure, with 3% - 5% of deaths (Verweyen et al, 2000).

Hematological and renal symptoms, including hemolytic anemia, low platelet counts, fragmentocytes, increased lactate dehydrogenase (LDH) and very low hemoglobin levels and various renal failure degrees may also be present. Other symptoms involved with other organs were brain, pancreas, myocardium, and malignant hypertension when associated with kidney failure and CNS involvement (Richardson et al, 1988). Salvadori and Bertoni (2013) in Italy highlighted the therapeutic aspects of HUS by the traditional therapy (including plasma therapy, kidney & kidney-liver transplantation) and new therapies (anti-Shiga-toxin antibodies & anti-C5 monoclonal antibody or Eculizumab®). They added that anti-C5 antibodies were more purified, less immunogenic, absorbed orally, and anti-C3 antibodies were more powerful, but less safe.

Pseudomembranous colitis: This rare, but serious disorder results from an overgrowth of toxin-producing clostridial organisms in the bowel. The typical presentation is acute watery diarrhea with lower abdominal pain, low-grade fever, and leukocytosis, starting during or shortly after antibiotic administration. The course can be fulminant, progressed from diarrhea to toxic megacolon and shock. Community-associated infection with a highly toxigenic strain of Clostridium difficile was reported in otherwise healthy children who had minimal or no exposure to antibiotics (Prince and Neu, 1979). C. difficile is an anaerobic, gram-positive, spore-forming, toxin-producing bacillus. In the environment, they survive in spores form, which are resistant to heat (even ordinary cooking heat), acid, antibiotics, and most antiseptics (Kim et al, 1981). Once the spores reach colon, they convert to the fully functional vegetative, toxin-producing form and become susceptible to killing by antimicrobial agents. Toxigenic strains were identified in healthy humans, food sources, farm animals, & pets, and hospital pet therapy dogs, and cultured from the environment in nursing homes, child care areas, and hospitals, particularly from the rooms of colonized or infected persons (Lefebvre and Weese, 2009). Many pediatric conditions have unique associations with C. difficile that may predispose to C. difficile infection, or exacerbated by C. difficile infection, or increase risk of severity or fatal C. difficile infection (AAP, 2009).

Conversely, however, as C. difficile colonization is common in children, the associations between fecal C. difficile toxin and intestinal symptoms may be completely incidental. Czepiel et al. (2019) found that the antibiotics of choice were vancomycin, fidaxomicin, and metronidazole, which was the least effective one. Mada and Alam (2022) updated the C. difficile infection management included a multi-step approach of discontinuing usage of inciting antibiotics, isolating the patient, and administering antibiotic based on infection severity. They added that antibiotics usually used were vancomycin or fidaxomicin. Asymptomatic patients with a positive stool toxin test didn’t require treatment. Metronidazole IV can be used for a patient suffered from ileus where orally administration of antibiotics was delayed.

Appendicitis: Appendicitis typically begins with diffuse abdominal pain followed by vomiting, always associated with constipation. Three most predictive clinical features are:
1- Pain in the right lower quadrant, 2- Abdominal wall rigidity, & 3- Periumbilical pain migration to right lower quadrant (Humes, 2006). Appendicitis was very common between ages of 10 & 20 years, but without age exempt. A male preponderance exists, with a male to female ratio of 1.4:1; overall lifetime risk was 8.6% for males and 6.7% for females in the USA (Addiss et al, 1990). Its’ diagnosis was missed in 3.8% to 15.0% of children and in 5.9% to 23.5% of adults during emergency department visits (Galai et al, 2017). Appendicitis is the second common disease condition among pediatric patients & the third common one in adult malpractice insurance claims (Brown et al, 2010). Mahajan et al. (2020) in USA found that factors associated with potentially missed appendicitis included female sex, the coexistence of abdominal pain and constipation, and presence of comorbidities. Becker et al. (2007) in USA reported that appendicitis in pediatric patients was difficult to diagnose as children presented with many different atypical clinical features, bowel problems, as bowel movement relieve discomfort. Appendicitis diagnosis as diarrheal cause may be delayed because the classic constellation of findings was absent, which was particularly true in young children or among any aged patients with a perforated appendix with long duration illness. Most people with appendicitis need the appendectomy. If appendix - re, surgery would prevent its rupture and keep infection from spreading. Before surgery, the patient must receive IV antibiotics to treat infection (AAFP, 2020).

Toxic megacolon: A complication of Shigella, pseudomembranous colitis, Hirschsprung disease, or inflammatory bowel disease (Jalan et al, 1969). Tsai et al. (2000) in Taiwan reported that toxic megacolon in infective colitis is a fulminating illness that has a high mortality rate, and can be divided into: acute toxic stage, gut failure stage, and convalescence or deterioration stage. Autenrieth and Baumgart (2012) in Germany found that the commonest causes included: a- Inflammatory (Ulcerative colitis, & Crohn’s disease), b- Infectious (Clostridium difficile, Salmonella, Shigella, Campylobacter colitis, Enterohemorrhagic or enteroaggregative Escherichia coli O157 that lead to hemolytic-uremic syndrome, Cytomegalovirus, & Entamoeba). Leifeld and Krüss (2012) in Germany reported that diagnosis easily done clinically, routine laboratory parameters and abdomen plain X-ray. They added that much difficulty was to decide between non-surgical treatment including intensive care treatment or surgery (mostly subtotal colectomy with terminal ileostomy). The non-surgical one included balancing of electrolytes and fluid volumes, broad-spectrum antibiotic as metronidazole®, positioning of patients and probably careful intermittent decompression.

Congenital secretory diarrheas: Congenital diarrheal disorders (CDDs) are group of inherited enteropathies characterized by profuse watery diarrhea began at or shortly after birth (Guarino et al, 1995), caused by a variety of inherited disorders that disrupt nutrient digestion, absorption, or transport, enterocyte development and function, or enteroendocrine function (Tab. 2). With the increasing use of whole-exome sequencing techniques, many more rare forms of congenital diarrhea are expected to be linked to genes contributing to appropriate intestinal fluid and electrolyte balance. An example for such discoveries was a mutation in diacylglycerol acyltransferase 1 (DGAT1), which catalyzes the final step in triglyceride synthesis; the mutation was detected associated with a familial form of congenital diarrhea in an Ashkenazi Jewish descent family (Haas et al, 2012). Mucosal biopsies must be done in patients with congenital diarrhea, which are a group of inherited enteropathies with a typical onset in early life, and such infants have frequently chronic diarrhea of sufficient severity for parenteral nutrition (Terrin et al, 2012). Undoubtedly, the results vary with etiology: 1- In the congenital chloride diarrhea (CCD) and congenital sodium diarrhea (CSD), with normal histology. Treatment was a high chl-
oride intake to prevent volume depletion. Determining optimal replacement dose was challenging because inadequate salt substitution paradoxically decreased diarrhea volume and excessive salt also increased diarrhea volume by osmotic mechanisms (Wedenoja et al, 2010). 2- In enteric endocrinosis, mucosal architecture was normal, but special stains demonstrate absence of enteroendocrine cells. 3- In tufting enteropathy, histopathology was characterized by villous atrophy, with disorganization of surface enterocytes and focal crowding; resembling tufts (Goulet et al, 2007). 4- In microvillus inclusion disease, light microscopy showed a variable degree of hypoplastic villus atrophy without crypt hyperplasia, & PAS-positive granules at the apical pole of enterocytes. Electron microscopy showed characteristic microvillus inclusions and partial to total atrophy of microvilli on mature enterocytes (Pecache et al, 2004), but in chylomicron retention disease, light microscopy may show lipid droplets in duodenal enterocytes. Whole-exome sequencing may be in select familial cases in which clinical, laboratory, and histologic examinations are non-revealing.

Osmotic diarrheas: They cease during fasting or upon exclusion of certain dietary components mal-digested by patient. 1- Glucose-galactose malabsorption presented by severe life-threatening diarrhea and dehydration during neonatal period, caused by deficiency in intestinal sodium/glucose transporter (Martin and Wright, 2004). Patients are symptomatic as long as the diet includes lactose or its hydrolysis products, glucose, and galactose. Diagnosis is suspected if diarrhea resolves promptly when these sugars are eliminated, confirmed by a positive glucose breath hydrogen test and normal intestinal biopsy. Treatment is with a fructose-based formula, and lifelong dietary restriction of causative sugars. 2- Congenital sucrase-isomaltase deficiency was rare in most populations, except in those of Eskimo or Canadian Native descent (Treem, 1995). Infants are asymptomatic if their diet contained only lactose (e.g., exclusively breastfed infants), but typically develop chronic diarrhea after sucrose-containing formulas or foods are introduced. Many mutations in gene encoding sucrase-isomaltase were described in affected patients, and well treated with sacrosidase (Lücke et al, 2009).

Evaluation: If a congenital diarrhea is suspected, stool electrolytes, pH, fat, & reducing substances must be measured, and a fasting trial must determine if it is secretory or osmotic. A marked decrease in stool output during fasting and high stool osmolality suggested an osmotic diarrhea. In suspected cases of bile acid malabsorption, measurement of total and specific bile acids from stool or utilizing the gamma emitter selenium-75-homocholic acid taurine (SeHCAT) may be considered, although these tests are usually not available on a clinical basis. Steatorrhea may also have osmotic mechanisms, but it tends to be lower volume and has a greasy rather than watery quality.

Conclusion

Two features of acute diarrheal illness, either alone or in combination, especially helpful in sorting via differential diagnosis are the fever and bloody or mucous diarrhea. Patient with acute diarrhea who requires volume resuscitation must be quickly identified. Clinical evidence of dehydration such as decreased urine output, tachycardia, and dry mucous membranes are already apparent at a deficit of 5% of body weight. Useful predicting signs for a volume deficit of 5%, or more include delayed capillary refill time > two seconds, reduced skin turgor, and deep respirations with or without an increase in respiratory rate, particularly if a combination of such findings was present. Moreover, identifying volume depletion, a thorough examination must be performed because the systemic, non-enteric infections, particularly otitis media, may cause acute diarrhea. A palpable mass or peritonitis suggests appendicitis, intussusception or, less commonly, toxic megacolon. Generalized toxicity and/or shock can occur with the hemolytic uremic syndrome or with sepsis, such as from the Salm-
onella and/or staphylococcal toxic shock syndrome.

Ancillary studies in children with acute diarrhea are based upon a good history and physical examination, an initial evaluation of a chronic diarrhea child in emergency setting.

References


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