Introduction

Acute gastroenteritis (GE) is a major cause of morbidity and mortality ***(Bryce et al., 2005).***

Viral pathogens are the most common causes of gastroenteritis (GE) in communities. The viruses that have been associated with GE are: Group A rotavirus (Rv-A), human caliciviruses (Hu CaVs), Noroviruses (NoVs) and sapoviruses (SaVs), human astroviruses (HAstVs) and human adenoviruses (HAdVs) ***(Vernacchio et al., 2006).***

Rotaviruses and noroviruses are the most important causative agents of viral GE. Rotavirus infection, are responsible for thousands of hospitalization of children worldwide ***(Parashar et al., 2006).***

Epidemiological studies demonstrated that P4, P8 and G1 to G4 rotavirus types are responsible for most of the rotavirus infections worldwide ***(Santos et al., 2005).***

NoVs require special cell systems for invitro replication ***(Straub et al., 2007).***

Among bacteria, Shigella SPP, and diarrheogenic Escherichea coli (DEC) are the most common causes of diarrheal diseases in developing countries ***(Davidson, 2002).***

Shigellosis still remains a public health problem in most developing countries because of the poverty, poor sanitation, personal hygiene and poor water supply ***(Iwalokun et al., 2001).***

It is a major cause of dysentery/ diarrhea in children and others. Many of them are hospitalized immediately after the onset of the disease ***(World Health Organization, 1998).***

Nontyphoid salmonella (NTs) is a common cause of bacterial GE which is usually a self-limited illness in healthy children that doesn't require antimicrobial treatment ***(Hohmann, 2001).***

As happens with most enteropathogens, there has been an alarming increase of resistance to different antimicrobial agents, and especially to those most commonly used in developing countries; such as ampicillin, trimethoprim/ sulfamethoxazole, chlormaphenicol or tetracyclines ***(Su, 2004).***

More rapid identification of the pathogen and its antibiotic sensitivity pattern could potentially guide antibiotic choice, reducing unnecessary use of expensive second-line antibiotics for susceptible isolates and

improving the outcome for multiresistant isolates and prevent morbidity and mortality ***(Miriagon et al., 2004).***

A cascade of cytokines coordinates the response to infection including tumor necrosis factor-α, interleukin-1 (IL-1), (IL-6) and (IL-8). Those proinflammatory cytokines play major roles in patho-physiology of infection and sepsis ***(Moldawer, 1994).***

Production of cytokines and proteins of the acute phase inflammation is often correlated with the severity of the bacterial infections ***(Sulliran, 1992).***

Aim of the Work

The aim of this study is to determine whether IL-6 is a marker capable of distinguishing between bacterial and viral gastroenteritis. So, early identification of the etiology of GE might obviate unnecessary use of antibiotics and prevent morbidity and mortality.

Gastroenteritis

Definition:

Gastroenteritis is a condition that causes irritation and inflammation of the GIT (the pathway responsible for digestion that include the mouth, esophagus, stomach and intestines ***(Benjamin, 2006).***

Signs and symptoms of gastroenteritis:

The main symptom is diarrhea but it may be accompanied by nausea, vomiting and/ or crampy abdominal pain ***(Arthur, 2008).***

Diarrhea:

Diarrhea is a problem not only of the developing world, but also of the western world. However the economic implications of diarrheal diseases are particularly evident in the poorer countries ***(Farthing et al., 2000).***

Diarrhea in children accounts for approximately 5 million deaths per year in the developing world. In United States, diarrhea accounts for 10% of all outpatient visits and 14 hospital admissions per 1000 children each year younger than one year of age ***(Ghishan et al., 2008).***

Diarrhea is an important cause of malnutrition, this is because patients with diarrhea eat less and their ability to absorb nutrient requirements is reduced, moreover their nutrient

requirements are increased as a result of the infection. Each episode of diarrhea contributes to malnutrition. When episodes are prolonged their impact on growth is increased ***(WHO, 1990-a)***.

Definition:

Vanderhoof (1999) defined diarrhea as the excessive loss of stool water and electrolyte. In infants, stool volume more than 15 gm/kg/24 h is considered diarrhea.Whereas by three years of age, stool output greater than 200gm/24h is considered diarrhea.

In breast fed infant who normally passes several soft or semi liquid stools each day, it is practical to define diarrhea as an increase in stool frequency or liquidity that is considered abnormal by the mother. On the other hand, greenish motion without change in stool consistency is not considered diarrhea and is of no significance ***(NCDDP, 1996).***

A diarrheal day was defined as the occurrence of ≥3 unformed stools (or ≥1 if bloody) in a 24 h period ***(Naficy et al., 2000).***

Classification:

Diarrheal diseases can be classified in various ways:

The first major subdivisions are acute, chronic and persistent Diarrhea ***(Farthing et al., 2000).***

Acute diarrhea implies a sudden onset, generally over hours rather than days and duration of less than one week,chronic diarrhea is generally of more gradual onset and lasts more than one to two weeks, whereas persistent diarrhea refers to diarrheal episodes of presumed infectious etiology that begins acutely but have an unusual long duration often more than fourteen days ***(WHO,1988 and Bhan et al.,1996).***

Pathophysiology:

Absorption of water from the small intestine is caused by osmotic gradient which is created when solutes (particularly sodium) are actively absorbed from the bowel lumen by the villous epithelial cells (Fig.1). There are several mechanisms whereby sodium is absorbed in the small intestine (Fig.2). To enter the epithelial cells, sodium is linked to the absorption of chloride ion or absorbed directly as sodium ion or exchanged for hydrogen ion or linked to the absorption of organic substances such as glucose or certain amino acids. The addition of glucose to an electrolyte solution can increase sodium absorption in the small intestine as much as three folds ***(WHO, 1990a).***

After being absorbed, sodium is transported out of the epithelial cells by an ion pump referred to as Na^+ K^+ ATPase. This transfers sodium into the extracellular fluid (ECF) elevating its osmolarity and causing water and other electrolytes to flow passively from the small bowel lumen through intercellular channels and into the ECF (Fig.2). This process

maintains an osmotic balance between fluid in the bowel lumen and the ECF ***(WHO, 1990a).***

1. Normal small intestine:

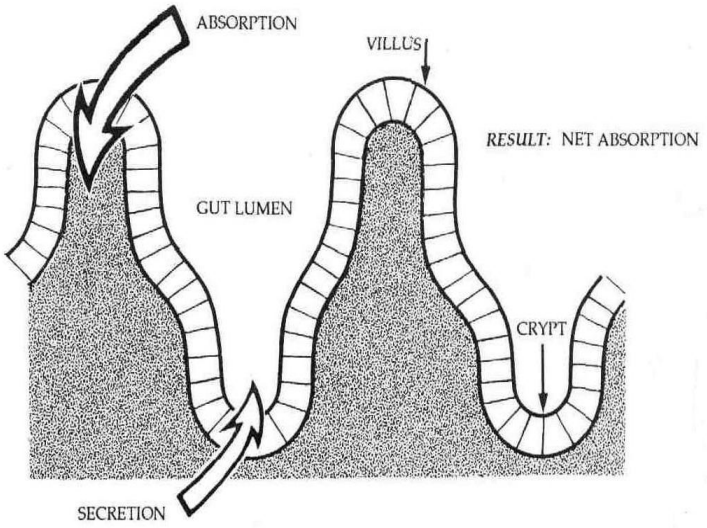

Fig. (1): Normal small intestine ***(WHO, 1990).***

2. Secretory diarrhea:

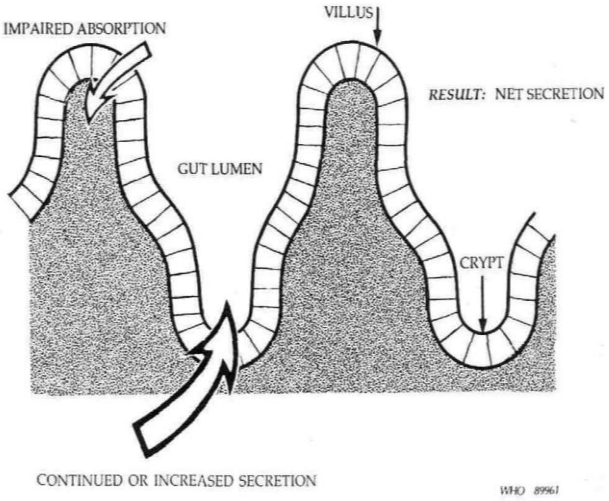

Fig. (2): Secretory diarrhea

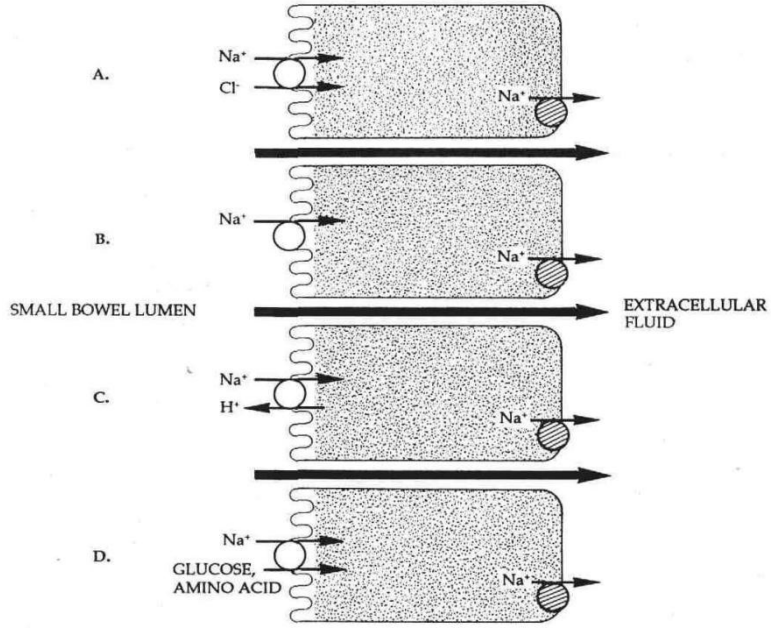

Fig. (3): Absorption and secretion of electrolytes and water by intestinal epithelium ***(WHO, 1990a).***

I. Sodium absorption in the villous epithelium

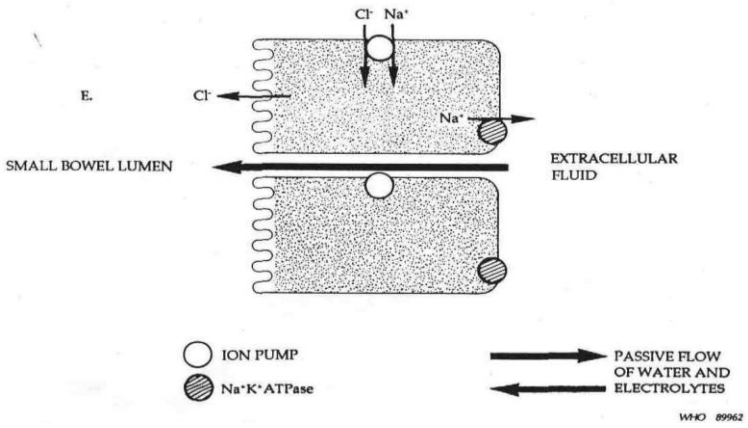

Fig. (4): Mechanisms of absorption and secretion of electrolytes and water in the small bowel epithelium ***(WHO, 1990a).***

II. Chloride secretion in the crypt epithelium

Pathogenesis:

The basis for all types of diarrhea is a disturbance in the intestinal solute transport, water movement across intestinal membranes is passive and is determined by both active and passive fluxes of solutes, particularly sodium chloride and glucose. The pathogenesis of most episodes of diarrhea can be explained by secretory, osmotic or motility abnormalities or a combination of these as shown in table (1) ***(Roy et al., 1995).***

A-Secretory diarrhea:

Secretory diarrhea can result from bacterial toxins, reduced absorptive surface area caused by disease or resection, luminal secretogogues (such as bile acids or laxatives), circulatory secretogogues (such as various hormones, drugs, toxins and poisons) and medical problems that compromise regulation of intestinal function ***(Schiller, 2000).*** These factors stimulate an abnormal secretion of water and electrolytes. As a result, there is little or no response to fasting ***(Roy et al., 1995).***

Table (1): Pathogenesis of diarrhea ***(Roy et al., 1995).***

Primary mechanism	Defect	Stool examination	Examples	Comment
Secretory	-Decrease absorption -increase secretion -electrolyte transport	Watery, Normal osmolality, Osmolality =electrolyle	-Cholera - toxoigenic Escherichiacoli -carcinoid -VIP - neuroblastoma -congenital chloride diarrhea -clostridium difficile -cryptosporidiosis - (AIDS)	Persists during fasting bile salt malabsorption may increase int estinal water secretion no stool leukocytes
Osmotic	-Maldigestion, -transport defect -digestive enzyme deficiency	Watery, acidic, +reducing substance	-Lactase deficiency	Stops with fasting increased breath hydrogen
	-ingestion of Unabsrbable solute	Osmolality >> electrolyte	Malabsorption -Laxative abuse	Carbohydrate malabsorpation. No stool leukocytes
Increased motility	Decreased transit time	Loose to normal appearing stool, stimulated by gastrocolic reflex	-Irritable bowel syndrome -Thyrotoxicosis -Postvagotomy -Dumping syndrome	Infection also may contribute to increased motility
Decreased motility	Defect in neuromuscular unit> stasis bacterial over growth	Loose to normal-appearing stool	Pseudo-obstruction. Blind loop	Possible bacterial over growth
Decreased surface area	Decreased functional capacity	Watery	-Short bowel syndrome. -Celiac disease -Rotavirus enteritis	May require elemental diet plus parenteral alimentation
Mucosal invasion	Inflammation -decreased colonic reabsorption -increased motility	Blood and increased WBCs in stool	-Salmonella -Shigella -Amebiasis -Yersinia -Campylobacter	Dysentery + blood mucus, and WBCs

VIP=Vasoactive Intestinal Peptide, WBC=White Blood Cell

B-Osmotic Diarrhea:

It occurs after ingestion of a poorly absorbed solute. The solute may be one that is normally not well absorbed (e.g. magnesium, phosphate or undigested unabsorbed sugar, alcohol, or sorbitol) or one that is not well absorbed because of the small bowel (e.g. lactose with lactase deficiency or glucose with rotavirus diarrhea ***(Roy et al., 1995).***

Malabsorbed carbohydrate is typically fermented in the colon and short chain fatty acids (SCFAs) are produced. Although (SCFAs) can be absorbed in the colon and used as an energy source, the net effect is to increase the osmotic solute load. This form of diarrhea is usually less in volume than the secretory diarrhea and stops with fasting ***(Roy et al., 1995).***

Comparison between osmotic and secretory diarrhea is shown in table (2)

Table (2): Differential diagnosis of Osmotic versus Secretory diarrhea ***(Ghishan, 2008)***

	Osmotic diarrhea	**Secretory diarrhea**
Volume of stool	<200 ml/24hr	>200 ml/24hr
Response to fasting	Diarrhea stops	Diarrhea continues
Stool Na+	<70 mEq /L	>70mEq /L
Reducing substances	Positive	Negative
Stool pH	<5	>6

C-Motility disorders:

Motility disorders may be associated with rapid or delayed transit, and generally are not associated with large volume diarrhea. Severe impairment of intestinal motility leads to intestinal stasis with subsequent bacterial overgrowth, bile acid deconjugation and malabsorption leading to diarrhea ***(Vanderhoof, 1999).***

Etiology of diarrhea:

Most cases of diarrheal diseases are due to the action of pathogenic organisms in the small or large bowel ***(Schiller, 2000).*** When diarrhea is presumed or actually shown to be secondary to a virus, a bacterial micro-organism or more rarely to a protozoan pathogen, the term infectious diarrhea is used ***(Roy et al., 1995).***

Risk factors of diarrhea:

1- Age:

Rotavirus diarrhea tends to be severe in patients 3-24 months of age. Although 25% of the cases of severe disease occur after 2years of age, with serologic evidence of infection developing in virtually all children by 4-5 years of age, infants younger than 3 monthes are relatively protected by transplacental antibodies and possibly breast feeding. Infection in neonates and adults in close contact with infected children is generally asymptomatic ***(Bass, 2008).***

2- Season:

In temperate climate, bacterial diarrhea occurs more during warm season, while viral diarrhea occurs more in winter ***(WHO, 1990-a).*** Rotavirus infection is most common in winter months in temperate climate ***(Bass, 2008).***

3- Malnutrition:

Malnutrition and micronutrient deficiency, particularly for zinc and vitamin A are known to increase the risk of prolongation of diarrheal episodes with higher mortality and morbidity. This is probably due to poor healing capacity of the intestinal epithelium and impaired immunity with inability of the body to eliminate the causative organisms ***(Soderndeo et al., 1997).***

4- Immune Deficiency:

Previous studies showed that children with impaired immune system evidenced by impaired skin test responses were more likely to develop diarrhea during follow up ***(WHO, 1988).***

Also, it was reported that children recovering from systemic infections e.g. measles were found to have increased incidence of diarrhea with long duration and high case fatality rates even in well nourished children ***(Bhan et al., 1996).***

Acute diarrhea or diarrhea in general may be associated with any of the infections or other causes listed in table (3).