

CHAPTER I

INTRODUCTION

Acute gastroenteritis is one of the most common diseases in infants, children, and adults worldwide. During the first 5 years of life, every child will contract diarrheal disease, which becomes the risk of dehydration and nutritional deficiency (Bern and Glass, 1994). Children in developing countries suffer from an average of 2.2-3.9 episodes of gastroenteritis annually (Snyder and Merson, 1982; Bern and Glass, 1994). Diarrheal disease can be severe particularly occurs among children in developing countries. In children under 5 years of age, it is responsible for 25-30% of all deaths (Martines et al., 1993; Bern and Glass, 1994). The annual mortality associated with gastroenteritis is estimated at 3.5-5 million, with the majority of deaths occurring in developing countries (Guerrant et al., 1990; Warren KS., 1990; Bern et al., 1993).

A variety of enteropathogens, including bacteria, virus, and protozoa are associated with gastroenteritis in all age groups (Leksomboon et al., 1981; Echeverria et al., 1994; Suwatano O., 1997). Since 1972, numerous of viruses were discovered as the causative agents of nonbacterial gastroenteritis. Globally, many different viruses have been detected in the stools of children with acute gastroenteritis, such as rotavirus (RV) 30-43 % (Barnes et al., 1998; Coluchi et al., 2002; Jiraphonhsa et al., 2005; Khamrin et al., 2006), norovirus (NV) 1.6-78.5 % (Nakayama et al., 1996; Greening et al., 2001; Schnagl et al., 2002; Subekti et al., 2002a; Lopman et al., 2003; Hansman et al., 2004b; Widdowson et al., 2004), sapovirus (SV) 3.3-48.0 % (Chiba et

al., 1980; Honma et al., 1998; Phan et al., 2004; Widdowson et al., 2004), Human astrovirus (HAstV) 0.3-14.0 % (Echeverria et al., 1994; Palombo et al., 1996; Pang et al., 1999b; Iritani et al., 2003), and enteric adenovirus 1-20% (Kidd et al., 1982; Herrmann et al., 1988; Moore et al., 1998; Saderi et al., 2002; Soares et al., 2002).

Norovirus (NV) or Norwalk-like virus is classified into the genus *Norovirus* in the family *Caliciviridae*. Norwalk virus is the prototype strain of noroviruses, previously called small round-structured viruses (SRSVs). In 1972, Kapikian et al. had detected virus particles, by electron microscopy (EM), in stool samples collected during outbreak of gastroenteritis in 1968 in Norwalk, Ohio (Kapikian et al., 1972). Subsequently, designated Norwalk virus, named for the town in Ohio where the outbreak occurred. Noroviruses can be divided into five distinct genogroups based on the variation in the capsid gene sequences, in which strains belong to GI, GII, and GIV are found in humans, whereas GIII and GV are found in cows and mice, respectively (Zheng et al., 2006). NV strains in each genogroup are classified further into genotypes or genetic clusters. NVGI and NVGII are predominant genogroups in humans and regard as the most diverse and common NV strains. The NVGI and NVGII strains have been classified, based on the difference of nucleotide sequences of partial capsid genes and segregated, into 15 (GI/1-GI/15) and 18 (GII/1-GII/18) genetic clusters, respectively (Okada et al., 2005). Furthermore, Zheng and colleagues (2006) had analyzed NVGI and NVGII strains based on amino acid sequences of complete capsid genes and showed that the GI and GII genogroups could be divided into 8 (GI/1-GI/8) and 17 (GII/1-GII/17) genotypes, respectively (Zheng et al., 2006). NVs are the major cause of outbreaks of gastroenteritis in institutions such as kindergartens, schools, nursing home, hospitals, and homes for the

mentally handicapped persons (Koopmans et al., 2003). In addition, NVs are also associated with sporadic cases of gastroenteritis among all age groups (Foley et al., 2000; Gallimore et al., 2004)

Sapovirus (SV) or Sapporo-like virus belongs to genus *Sapovirus* in the family *Caliciviridae*. The prototype strain of human SV, the Sapporo virus, was originally discovered from an outbreak of gastroenteritis in an orphanage in Sapporo, Japan, in 1977 (Chiba et al., 1979). Sapporo virus has a morphologic appearance similar to a typical animal calicivirus which contains cuplike depressions and spikes on the particle surface, called a “Star of David” appearance (Chiba et al., 2000). Recently, SV strains are divided into five genogroups (GI to GV) based on the difference of capsid gene sequences, of which GI, GII, GIV, and GV are found in humans, while GIII is found in porcine species (Farkas et al., 2004). SV strains in each genogroup are classified further into genotypes or genetic clusters. SVs are the causative agent of outbreaks of gastroenteritis in institutions such as infant homes, hospitals, and health centers (Nakata et al., 2000; Okada et al., 2002). In addition, SVs are also associated with sporadic cases of gastroenteritis among infants and children (Madeley and Cosgrove, 1979; Hansman et al., 2004b; Phan et al., 2005), although infection of adults and elderly persons also occur (Atmar and Estes, 2002).

Human astroviruses (HAstVs) and animal astroviruses are the members of the genus *Astrovirus*, family *Astroviridae*. HAstVs were first observed by EM in stool specimens from infants with gastroenteritis (Madaley and Cosgrove, 1975). These viruses are small in size and icosahedral in shape, and they are named based on their characteristic starlike surface structure (*astron*, "star" in Greek). HAstVs can be divided into eight distinct serotypes or genotypes based on the antigenic difference or

the variation in the capsid gene sequences: serotype/genotype 1 to serotype/genotype 8, in which a high concordance between results of serotyping and genotyping was observed (Sakamoto et al., 2000). HAstVs are commonly associated with outbreak or sporadic gastroenteritis in children and adults (Utagawa et al., 1994).

In Thailand, epidemiological studies of NV, SV, and HAstV are less frequent than those of RV. In 1980, a serological study performed by Echeverria and colleagues in the northeastern area of Thailand revealed that 70% of children had already acquired antibody to Norwalk virus during the first 4 to 5 years of age (Echeverria et al., 1983). During January 1982 to May 1983, the small round virus-like particles were first detected in Thailand by EM from children at the age of 1 month to 5 years who admitted to two hospitals in Bangkok (Wasi et al., 1984). In 1990, Herrmann et al. (1991) using an indirect double-antibody ELISA with monoclonal antibody could detect HAstV at 8.6% in stool specimens from diarrheic infants and children under 5 years of age who attended the clinics in Bangkok. Later, in 1991, Echeverria et al. (1994) reported the detection of HAstV at 14% in stool specimens of children under 5 years of age with acute diarrhea who admitted to hospital and clinics in Ratchaburi. Guntapong et al. (2004) had reported 11 (14%) NV and 9 (11%) SV single infections, and 3 (4%) NV/SV mixed infections in a total of 80 stool specimens collected from children hospitalized with acute gastroenteritis in 4 regions of Thailand as detected by reverse transcription-polymerase chain reaction (RT-PCR). Analysis of partial capsid sequences of NV or SV revealed that majority of NV strains belonged to NVGII/4 (64%) but none belonged to NVGI, while most of SV strains belonged to SVGI (83%), respectively. Moreover, one isolate of SV represented a novel genogroup (GV) within the SV genus. In 2004, a

report from Bangkok demonstrated the relevance of HAstV as a cause of neonatal gastroenteritis outbreak occurred in nursery of a maternity ward of Ramathibodi Hospital. HAstV was detected, by ELISA, in 4 of 13 (30.7%) of diarrheic neonates and in 1 member of nursery staff who had diarrhea (Sirinavin et al., 2006). The preliminary study of NV and SV infections among infants and children under 5 years of age with diarrhea had been performed in Chiang Mai in 2002 (Hansman et al., 2004b). In that study, NV infection was 7.6% while SV infection was 3.8%. One specimen (0.95%) was a NV/SV mixed infection. However, HAstV infection was not determined in that study.

Therefore, it is of interest, to do follow-up investigation the prevalence and distribution patterns of NV, SV, and HAstV infections among children hospitalized with acute gastroenteritis in Chiang Mai. Moreover, we analyze the capsid gene sequences of these viruses and compare to those of reference strains to identify the genogroup and genotype of these viruses. In addition, the information gained from this study might help to elucidate molecular epidemiology of these viruses in Thailand.