

# Epidemiologic studies on human enteric viruses in Cameroon

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This thesis is based on the following studies, referred to in the text by their Roman numerals.

- I. Ayukekbong J, Lindh M, Nenonen N, Tah F, Nkuo-Akenji T, Bergström T. **Enteric viruses in healthy children in Cameroon; viral load and genotyping of norovirus strains.** *J Med Virol* 2011; 83:2135-41.
- II. Ayukekbong J, Kabayiza J, Lindh M, Nkuo-Akenji T, Tah F, Bergström T, Norder H. **Shift of Enterovirus Species among Children in Cameroon – Identification of a new enterovirus, EV-A119.** *J Clin Virol* 2013; 58:227-32.
- III. Ayukekbong J, Andersson ME, Vansarla G, Tah F, Nkuo-Akenji T, Lindh M, Bergström T. **Monitoring of seasonality of norovirus and other enteric viruses in Cameroon by real-time PCR; an exploratory study.** *Epidemiol Infect* 2013. 1-10.
- IV. Ayukekbong J, Fobisong C, Lindh M, Nkuo-Akenji T, Bergström T, Norder H. **Molecular analysis of enterovirus in Cameroon by partial 5'UTR-VP4 gene sequencing reveals a high genetic diversity and frequency of infections.** *Submitted.*

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UNIVERSITY OF GOTHENBURG

# Epidemiologic studies on human enteric viruses in Cameroon

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Enteric viruses are a diverse group of viruses that include those that multiply in the intestinal epithelium and cause gastroenteritis, and those that first multiply in the intestine and then spread to extra-intestinal target organs where they cause other diseases. Noroviruses and enteroviruses fall within the former and the latter category respectively. Noroviruses are considered to be the most common cause of acute non-bacterial gastroenteritis in both children and adults in industrialized countries. Enteroviruses may induce diseases of varying severity ranging from conjunctivitis, acute flaccid paralysis, encephalitis, aseptic meningitis, and hand, foot and mouth disease. The risk of infection by enteric viruses is higher in sub-Saharan Africa compared to developed countries probably due to sub-optimal sanitation and hygienic conditions as well as to low quality of drinking water especially in rural areas. In Cameroon, very limited studies have been carried out on the epidemiology of these viruses. Globally, comprehensive prospective data on the dynamics of circulation of noro- and enteroviruses are scarce. There are no vaccines or therapeutics for norovirus infections, therefore advanced knowledge of the epidemiology is necessary for adequate prevention and control of the disease. Both viruses are transmitted by the fecal-oral-route, and an important feature of these viruses is the silent shedding in asymptomatic persons which may facilitate the transmission to susceptible persons. This thesis is focused on the seasonality, genetic diversity and dynamics of circulation of noro- and enteroviruses in Cameroon.

Fecal samples were collected from participants and enteric viruses were detected by an in-house multiplex real-time PCR assay. Norovirus genotyping was achieved by RdRp-N/S genomic region sequencing, while enterovirus identification and typing was done by amplification of the 5'UTR-VP4 and partial VP1 regions of the genome respectively. To investigate the sequence diversity and strain circulation, all the sequences were subjected to phylogenetic analysis.

A high prevalence and diversity of enteric viruses among children and adults was observed which was associated with a high frequency of infections with different strains. Up to five different enteric viruses were detected in a healthy child at a single observation. In a longitudinal follow-up, 1-5 (mean 2.0) different enterovirus infections occurred in children within a year. The study reveals the first description of norovirus in Cameroon and the discovery of a novel enterovirus type designated EV-A119. There was no statistical difference in the detection of norovirus in persons with diarrhea and in those without diarrhea suggesting that, although noroviruses are highly prevalent, they may not be a major cause of diarrhea in the study population. The observed shift in the predominant enterovirus species or norovirus genogroup from one period to the other, and prolonged viral excretion of up to 10 months for enterovirus in asymptomatic persons has great public health implications in the control of diseases caused by these viruses. This study also revealed a strong association between rainfall and the prevalence of noro- and enteroviruses.

Taken together, the high degree of circulation of diverse noro- and enteroviruses in a healthy population in Cameroon suggests silent shedding of these viruses into the environment and eventual contamination of sources for drinking water. These naturally circulating noro- and enteroviruses may induce strong innate and adaptive immune responses and raise question whether these viruses may constitute components of the intestinal 'virobiota'. Conversely, the detection of naturally circulating rotaviruses was low. This may explain why rotavirus detection in feces has been strongly associated with diarrheal disease.

The obtained insights into the dynamics of circulation of these viruses can hopefully be used to develop adequate preventive and control strategies in order to eliminate symptomatic infections caused by these viruses.

**Keywords:** Norovirus, enterovirus, molecular epidemiology, seasonality

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