

**ACUTE GASTROENTERITIS IN RWANDAN CHILDREN UNDER FIVE YEARS OF  
AGE INVESTIGATED BY REAL-TIME PCR**

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by

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This thesis is based on the following papers:

**I: Jean-Claude Kabayiza**, Maria E Andersson, Christina Welinder-Olsson, Tomas Bergström, Gregoire Muhirwa and Magnus Lindh. Comparison of rectal swabs and faeces for real-time PCR detection of enteric agents in Rwandan children with gastroenteritis. *BMC Infectious Diseases* 2013, 13:447.

**II. Jean-Claude Kabayiza**, Maria E Andersson, Staffan Nilsson, Cyprien Baribwira, Tomas Bergström, Gregoire Muhirwa, Magnus Lindh. Real-time PCR identification of agents causing diarrhoea in Rwandan children under five years of age. Submitted manuscript.

**III. Jean-Claude Kabayiza**, Maria E Andersson, Staffan Nilsson, Cyprien Baribwira, Gregoire Muhirwa, Tomas Bergström, Magnus Lindh. Clinical and epidemiological characteristics of microbes causing more severe infectious diarrhoea identified by real-time PCR in children under five years of age in Rwanda. Manuscript.



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## ABSTRACT

Acute gastroenteritis is a major cause of illness and death among children in developing countries. Knowledge about the aetiology is important to make the right priorities regarding preventive measures, and for the recommendation to use or not use antibiotics. The objective of this thesis was to investigate causes of acute diarrhea in children in Rwanda by real-time PCR targeting a wide range of infectious agents.

By analysing 326 paired faecal samples we found that rectal swabs provided equal rates of PCR detection of 10 different pathogens as usual stool samples, and correlating Ct values indicated that rectal swabs also may be used for quantitative measurements.

PCR findings in 544 children with acute diarrhea and 162 controls showed a higher prevalences in children with than without diarrhea only for rotavirus and the enterotoxigenic *E. coli* (ETEC-estA) (42% vs. 2%, and 21% vs. 9%). Other agents were detected at similar rates in sick and healthy children (adenovirus, 39% vs. 36%; ETEC-eltB, 29% vs. 30%, *Campylobacter*, 14% vs. 17%, *Shigella*, 13% vs. 10%). Lower Ct values for ETEC-estA, *Shigella* and norovirus GII indicate that measuring pathogen concentration in faeces may help to identify clinically relevant infections.

At least one pathogen was detected in 92% of 880 children with diarrhea. Rotavirus and ETEC-estA were associated with more severe dehydration, *Shigella* with bloody diarrhoea and higher CRP, and concentrations in faeces of rotavirus, ETEC-estA and *Shigella* were associated with more severe symptoms. Rotavirus and ETEC-estA were more common in younger, *Shigella* more a common in older children. Antibiotics were given to 42% of children, mainly those with fever and more severe dehydration, and without any logical connection with the causative organism.

The conclusions of this thesis are (i) that rectal swabs are as good as conventional stool samples for pathogen detection by PCR, (ii) that rotavirus, ETEC-estA and *Shigella* were the major causes of gastroenteritis, (iii) that higher concentrations of rotavirus, ETEC-estA, *Shigella* and norovirus GII were associated with symptoms, and that Ct value cut-offs for these agents improved identification of them as causes of disease, (iv) that antibiotics were used extensively and in a seemingly irrational manner, and (v) highly sensitive multiple real-time PCR was efficient and informative and that its use in future studies may provide valuable new information about the clinical significance and epidemiology of these infections.

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