HIV-infection in sub-Saharan Africa
From quantity to quality of care

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Chapter 8

Summary
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Until today the HIV-virus has infected over 70 million people worldwide (1) in one of the biggest global health challenges ever faced. In 2018 this included a total of 1.8 million children (age < 15 years) with almost ninety percent of these children living in sub-Saharan Africa (2,3). Over the last decade important steps have been taken worldwide to improve HIV care for adults and children, including in sub-Saharan Africa.

Now that ART has become more accessible (4-6), further progress in the fight against HIV will require the determination of health care providers and policymakers to further increase the quantity of those receiving treatment, alongside improvement in the quality of HIV care in sub-Saharan Africa. In addressing the HIV pandemic, the quality of HIV care will become increasingly important as resistance to HIV drugs is rising. This thesis focused on multiple aspects of the care of HIV-infected children and adults living in sub-Sahara Africa and aimed to gain further insight into optimal HIV treatment in order to improve long-term survival for these patients: HIV-infection in sub-Saharan Africa; from quantity to quality of care.

Summary | Treatment and monitoring

The first part (Part 1) of this thesis focused on HIV treatment, with special attention paid to initiation and monitoring. During the last decade, many aspects of HIV care have improved. Specifically, with widespread implementation of the World Health Organization’s “treat all” recommendation in 2016, all HIV-infected patients receive ART regardless of age or CD4 counts. Previously, as CD4 counts were regularly not available, clinical criteria were used to start ART. As a result, patients were identified late. The results of our prospective cross-sectional study on HIV-infected Malawian children, who were not eligible for ART based on clinical criteria as reported in Chapter 2, indicated that there are no adequate clinical markers to replace CD4 counts. This negative finding has provided support for the current “treat all” approach. In Chapter 3 and Chapter 4 we described the short and long-term treatment outcomes for children on ART and focused on HIV drug-resistant mutations. Chapter 3 reported data from a prospective cohort of HIV-infected Malawian children with high rates of HIV drug resistance and treatment failure after the first year of ART. These results emphasized the need for paediatric HIV treatment
programs to improve treatment follow-up that, even in low resource settings, should include regular viral load testing to allow adequate treatment switches and reduce the further development of resistance. **Chapter 4** presented long-term follow-up data (4 years) from a paediatric multicentre cohort of HIV-infected children on first-line ART in Uganda. Using this we reported a high prevalence of treatment failure and resistance to HIV drugs in one of the very few long-term datasets from Africa. Treatment failure occurred predominantly in the first 24 months. However, a second increase in treatment failure incidence occurred at year four. Children whose treatment had failed in the first 24 months had different risk factors, with greater occurrence of early treatment failure patterns and acquired HIV drug resistance mutations than children whose treatment failed after 24 months. These findings suggested that children with treatment failure in the first 24 months may benefit from repeated viral load monitoring and prompt switching to second line treatment, whilst treatment failure after 24 months may be prevented by earlier commencement of ART, which again supports the “treat all” recommendations of the World Health Organization.

**Summary | HIV-infection in sub-Saharan Africa; co-morbidities**
The second part of this thesis (**Part II**) focused on co-morbidities of HIV-infected children and adults in sub-Saharan Africa. Diarrhoea is an important cause of mortality in children under the age of five worldwide and highly common in HIV-infected children. In **Chapter 5**, using PCR techniques, we described the prevalence and clinical relevance of specific intestinal protozoa in HIV-infected Malawian children with diarrhoea before and during their first year of ART. Surprisingly, we found that a relatively unknown opportunistic pathogen, E. bieneusi, was the most prevalent opportunistic intestinal protozoa, and was present in over a third of study participants prior to the initiation of ART. Although all children were clear of E. bieneusi after 12 months of ART without specific treatment, E. bieneusi and its treatment may be of clinical importance as it was associated with initial gastrointestinal complaints and a potentially delayed BMI recovery over 12 months of follow-up.

Severe anaemia is a major cause of morbidity in HIV-infected patients in LMIC and is associated with increased mortality. Previously, our research group reported on a large dataset involving children with severe anaemia in Malawi, including those
who were HIV-infected. However, comprehensive data on the aetiology of HIV-associated severe anaemia in adults especially on ART is lacking (7). In Chapter 6 we reported the results of a comprehensive observational study that explored the mortality and potential aetiologies of HIV-associated severe anaemia (Hb≤70 g/L) in Malawian adults. In our population, mortality among severely anaemic HIV-infected adults was strikingly high (50%); suggesting that severe anaemia in HIV-infected adults must be investigated and treated urgently. In addition, all of the adults in the study averaged three potential aetiologies of (severe) anaemia, indicating that the aetiology of severe anaemia in this population is multifactorial, with several coinciding diseases occurring. This highlights the need for clinicians to be wary of the possibility that multiple causes of severe anaemia must be identified and treated.

Iron deficiency has always been regarded as a primary cause of (severe) anaemia in LMIC. In the search for the aetiology of severe anaemia in HIV-infected patients we identified in Chapter 6 that iron deficiency may be an important contributor to the development of severe anaemia, as it was prevalent in 55% of our population. In a sub-study presented in Chapter 7, we evaluated and described the difficulties of diagnosing bone marrow iron deficiency using peripheral blood markers in this specific patient population. The study showed that these markers performed poorly in determining iron deficiency in this group of patients. Hepcidin, a specific hormone in metabolising iron, did perform slightly better than conventional markers and this might aid the decision as to whom iron supplements may be safely and effectively prescribed.
References


