1. Introduction

Human immunodeficiency virus (HIV) infection has been pandemic for the last 30 years and continues to be a major global public health issue (1). In 2017, 1.8 million people were newly infected with HIV and an estimated 36.9 million people were living with HIV worldwide (2). Sub-Saharan Africa is at the epicenter of the epidemic and continues to carry the health and socioeconomic impact of the HIV epidemic, with 25.7 million people living with HIV in Africa in 2017 (2).

Treatment for cure or an effective vaccine has not been yet found for HIV. However, there is a significant advance in HIV treatment since the first antiretroviral drug, zidovudine (AZT), was approved for treatment of acquired immunodeficiency syndrome (AIDS) in 1987 (3). The development of a number of antiretroviral (ARV) drugs and the transition from a one drug treatment to combination of three drugs treatment concept for HIV infection has brought impressive benefit in reducing HIV related morbidity and mortality (4). Moreover, the better understanding of benefits of early initiation of combination antiretroviral treatment (ART) has led to an improvement in ART coverage (5). For the first time ever in 2017, more than 50% of the global population living with HIV were receiving ART (2).

Expanded access to ART has led to a decline in AIDS-related deaths globally (6). In 2017, there was a 38% reduction in death annually relative to year 2000 (2). However, an increase in non-AIDS related morbidity and mortality due to non-AIDS malignancies, cardiovascular, pulmonary, chronic liver and kidney disease was reported in HIV patients when compared to the general population (7–12). A number of reasons have been reported for an increase in non-AIDS morbidities in HIV patients like aging, drug toxicities, coagulation activation, persistence inflammation and immune dysfunction (13–15).

Vitamin D is important for regulation of the immune system and reduction of inflammation in the body (16,17). Studies have indicated that HIV Positive persons with low Vitamin D levels have been associated with disease progression and mortality (18,19). Moreover, some ARV drugs affect vitamin D metabolism and may lead to further reduction (20,21). The current direction pointed to restoration of vitamin D to normal values during treatment with ART in HIV positive
persons with vitamin D supplementation (22). This underlines the need to study further vitamin D levels and the effect of vitamin D supplementation on serum vitamin D level during ART in HIV positive persons living in different geographical location and climates.

ARV drug toxicity in HIV positive persons is one of the contributing factors for an increase in non-AIDS morbidity (23). Most ARV drugs can result in kidney injury with long term use and when provided with combination of other drugs (24,25). In contrast, ART is the mainstay treatment for HIV associated nephropathy (HIVAN) (26). HIVAN is common in black race and it is the third leading cause of nephropathy in the population of African descent (27). Hence, this could indicate the need for appropriate screening and monitoring of kidney function pre and post ART in HIV positive persons. However, the limited diagnostic facilities for determination of renal function and the lack of validated equation for estimated glomerular filtration rate (eGFR) in most low and middle income countries may hamper early diagnosis of renal disease in HIV patients (28). Besides, there are limited facilities for managing end stage renal disease (ESRD) in low and middle income countries which may further reduce survival time (29–31). Therefore, studies that show the extent of renal disease in ART naïve and ART experienced African HIV positive persons and identify factors that worsen renal disease or result in kidney injury have paramount importance. Such data will not only help to develop strategies to early identify and prevent kidney injury in HIV positive persons but also for efficient use of renal function tests for screening and monitoring in resource limited settings.

This PhD thesis is based on data from a cohort of HIV positive adults enrolled in a nutritional intervention trial in (“ARTfood study”) in Ethiopia.