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Relationships Between Adverse Childhood Experiences and Clinical Outcomes Among Adolescents Living with Perinatally Acquired HIV: A Mixed-Methods Analysis

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2017

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Abstract

Relationships Between Adverse Childhood Experiences and Clinical Outcomes Among Adolescents Living with Perinatally Acquired HIV: A Mixed-Methods Analysis

By Emma Clevenger

Background: Globally, adolescents living with HIV (ALHIV) bear a disproportionate burden of the HIV epidemic and this disparity is more pronounced in low-resource settings. In addition to increased risk of poor health outcomes, ALHIV are also more likely to experience adverse childhood experiences (ACEs). ACEs have been shown to have negative impacts on mental and physical health. Given the growing population of ALHIV, there is a need to better understand their challenges and lived experiences of this population, including ACEs and their impact on HIV care.

Objective: This study aimed to understand the effects of ACEs on the health of perinatally infected ALHIV, from the perspective of adolescents, caregivers, and providers; explore the relationship between ACEs and virological outcomes among ALHIV; and explore strategies that foster resilience among ALHIV following adversity, including the mitigating role of social support.

Methods: 130 randomly selected ALHIV engaged in care at study sites in Western Kenya participated in a survey. Purposive sampling was used to select 45 of these adolescents for focus groups (FGDs) (n=30) or in-depth interviews (IDIs) (n=15). Ten caregivers to ALHIV and 15 healthcare providers were recruited for additional interviews. Descriptive statistics and tests of association were used to assess relationships between ACEs and clinical outcomes; thematic analysis was used to identify recurring themes in the FGD and IDI data.

Results: The prevalence of ACEs was high, with a mean of 1.2 (SD=1.8) ACEs experienced by ALHIV. Several ACEs were significantly associated with poorer virological or clinical outcomes, and results varied by gender. A number of themes emerged from the qualitative findings, in which all participant types spoke of ALHIV experiences with abuse, neglect, and household challenges, and potential mitigators were proposed based upon personal experiences or observations.

Conclusions: Findings suggests that ACEs may negatively impact the later clinical outcomes of adolescents living with perinatally acquired HIV. Additional research is necessary in order to elucidate the pathways between ACEs and negative health outcomes in this population, and to further inform programs and policies to prevent ACEs and reduce their impact on engagement in care and the health and well-being of ALHIV.

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Table of Contents

Chapter I: Introduction

1.1 Introduction and Rationale

According to most recent estimates, approximately 1.8 million adolescents between the ages of 10 and 19 worldwide are living with HIV, acquired either perinatally or horizontally. This group suffers from the highest AIDS-related mortality with 32,000 adolescents dying from AIDS-related causes in 2020 (UNICEF, 2021). While this is the eighth leading cause of adolescent mortality globally (Slogrove & Sohn, 2019), it is the top cause of death among adolescents in Kenya (Republic of Kenya Ministry of Health, 2015). Of the 141,000 adolescents living with HIV (ALHIV) in Kenya, nearly 3,000 die of AIDS-related illnesses each year (Elizabeth Glaser Pediatric AIDS Foundation, 2018).

Due to successful prevention of mother-to-child transmission (PMTCT) programming, the number of new perinatal HIV infections has decreased significantly; however, the population of ALHIV continues to grow as more children who acquired HIV perinatally survive into adolescence through expansion of antiretroviral therapy (ART) availability and as a result of the overall reduction in child mortality in recent decades leading to the largest ever cohorts of adolescents in Africa. ALHIV in Kenya have been shown to have poorer adherence to ART regimens and therefore lower rates of viral suppression than other age groups (Luseno, et al., 2017), and they are at a greater risk of being lost to follow-up and dying than children and adults with HIV. Adolescents with perinatally acquired HIV experience a unique set of challenges that face an increased likelihood of having advanced disease, opportunistic infections, and mental health problems than those that acquire HIV horizontally. These adolescents face a lifetime of ART use, and therefore are at a higher risk of treatment failure and subsequent mortality (Slogrove & Sohn, 2019).

Further complicating their treatment, perinatally infected ALHIV are more likely to face a number of challenges, including the loss of a parent or a parent experiencing severe illness, death of a sibling, poverty, housing instability, and stigma (Agwu & Fairlie, 2013). These events, known as adverse childhood experiences (ACEs), have been widely studied among high-income populations and shown to have significant impacts on physical and mental health (*About the CDC-Kaiser ACE Study |Violence Prevention|Injury Center|CDC*, 2021). Research on the effects of ACEs in low-income settings is severely lacking and few studies examine the consequences of ACEs among ALHIV. This research could have implications for how to best anticipate and address the challenges faced in treating adolescents for HIV, and add to the growing evidence to support trauma-informed care models.

1.2 Problem Statement

Although adolescents bear a disproportionate burden of the HIV epidemic, research specific to this population is limited. Furthermore, existing research seldom differentiates between horizontally or vertically infected adolescents despite each group facing unique challenges. With many perinatally infected ALHIV in sub-Saharan Africa experiencing childhood adversity, there is a need to understand how this impacts their ability to manage their illness during adolescence.

1.3 Purpose Statement

Despite continuing research on the impacts of ACEs and advocacy for adolescent-tailored HIV care, research on the impacts of ACEs among ALHIV is severely limited, particularly in low-income settings and in sub-Saharan Africa specifically. This study will fill the gap in research that is necessary to understand the relationship between ACEs and adolescents' experience with HIV management and clinical outcomes.

1.4 Objectives

1. Understand the effects of adverse childhood experiences on the health of perinatally infected ALHIV from the perspective of adolescents, caregivers, and providers.

2. Explore the relationship between adverse childhood experiences and virological outcomes for ALHIV.
3. Explore strategies that have fostered resilience among ALHIV following childhood adversity and the mitigating role of social support.

1.5 Significance Statement

This study will provide a better understanding of the impacts of childhood adversities on HIV outcomes among perinatally infected adolescents in Western Kenya. If utilized, this research has the potential to inform best practices in caring for ALHIV and identify strategies to mitigate the effects of ACEs among this population in Kenya and other lower-resource settings.

1.6 Definition of Terms

Adolescent: a person in a transitional period between a child and an adult aged 11 to 19 years.

Perinatally (vertically) acquired HIV: HIV infection that is transmitted from a mother to a child during pregnancy, birth, or while breastfeeding.

Behaviorally (horizontally) acquired HIV: HIV infection that is transmitted through sex or sharing of contaminated objects, such as needles.

Virological outcomes: measurements of HIV treatment status including viral load and viral suppression.

Adverse childhood experiences: traumatic events that occur during childhood from ages 0 to 17 years that include abuse, neglect, witnessing violence, parental separation, exposure to substance use problems, exposure to mental illness, or death of a parent or sibling.

ACE: Adverse childhood experience

ALHIV: Adolescent(s) living with HIV

ART: Antiretroviral therapy

LTFU: Loss to follow-up

PEPFAR: President’s Emergency Plan for AIDS Relief

PMTCT: Prevention of mother-to-child transmission

PLHIV: Person/People living with HIV

Chapter II: Literature Review

2.1 Introduction

The purpose of this chapter is to review the existing published literature and research on factors impacting engagement in care and related health outcomes of adolescents living with perinatally acquired HIV in the context of Kenya and similar low-income, sub-Saharan African settings. In conducting this review, a variety of sources were used including academic journals and governmental reports. While the focus of this review was on ALHIV in Kenya, data from other areas was utilized when appropriate due to generalizability or, in the case of using research from high-income settings, comparable study design. The review provides a comprehensive summary of negative health outcomes associated with ACEs and factors impacting clinical outcomes among ALHIV with a focus on this population in sub-Saharan Africa and identifies current gaps in research.

2.2 Adolescents living with HIV in Kenya

Research specific to adolescents living with HIV (ALHIV) is severely lacking, despite this population accounting for an estimated 2.1 million infections globally (Armstrong, et al., 2018). Eighty-four percent of ALHIV are living in sub-Saharan Africa, and 90% of ALHIV deaths occur among the same population. Due to successful prevention of mother-to-child transmission (PMTCT) programs the number of new perinatal infections has substantially decreased, however the population of ALHIV is growing as more perinatally infected children survive into adolescence through widespread expansion of ART availability and the reduction in overall child mortality in the previous thirty years, leading to the largest ever adolescent cohorts (UNICEF, 2017). Both vertically and horizontally infected ALHIV are at greater risk of being lost to follow-up and dying than children and adults with HIV, a phenomenon that is often attributed to the challenges of navigating the complexities of the transitional period of adolescence while managing a chronic illness, further complicated by the burden of stigma and social challenges

(Slogrove & Sohn, 2018). Older adolescents typically demonstrate poorer adherence than younger ALHIV, with those over the age of 15 at a higher risk of non-adherence (Agwu & Fairlie, 2013). Despite HIV programs recognizing adolescents as a critical age group with a unique and diverse set of challenges, research concerning this population and how to best meet their needs is lacking globally, and more severely so in low-resource settings.

With an estimated 130,000 infected adolescents and 18,000 new infections per year, Kenya contributes significantly to the global burden of HIV among adolescents (Luseno, et al., 2017). Within the country, HIV remains the leading cause of death for adolescents (ages 10-19) and young people (ages 19-25). Research concerning ALHIV in Kenya is severely lacking but in the studies that have been conducted, the findings are largely consistent with those in similarly low-resource Eastern and Southern African countries. One such finding is that Kenyan ALHIV are more likely to be lost to follow-up than older or younger groups with HIV. Additionally, studies have shown that ALHIV in Kenya demonstrate poorer adherence to ART and therefore lower rates of viral suppression than other age groups (Luseno, et al., 2017).

Due to increased recognition of the vulnerability of ALHIV and the need for tailored programming, a number of qualitative studies have been conducted examining their lived experiences and engagement in care. Several (Enane, et al., 2020, Hall, et al., 2016, Williams, et al., 2017) have identified stigma and isolation as significant barriers to care engagement. One study conducted in Coastal Kenya found additional challenges resulting from poverty, mental health issues, and unsupportive school systems. Researchers used a cross-sectional qualitative study design with semi-structured key informant interviews with ALHIV, HIV-uninfected adolescents, and other key informants including health service providers, community health workers, and secondary school teachers (Abubakar, et al., 2016). Despite this growing body of research, notable gaps remain, leaving ALHIV without adequately tailored services to support them to continue engagement in care while navigating the transitional period of adolescence.

2.3 Perinatally infected adolescents living with HIV

Although the experiences of those with perinatally acquired HIV have been studied in resource-rich countries (Neilan, et al., 2018; Judd, et al., 2016; Judd, et al, 2018), few studies have been done in low-resource settings with a focus specific on perinatally infected individuals, including adolescents. Epidemiological studies concerning perinatally acquired HIV are lacking as global and national reporting does not differentiate between vertical and horizontal infections among youth, making it difficult to track their outcomes on a large scale. Because of this, most research about perinatally infected ALHIV relies on local or regional cohort surveillance (Sohn & Hazra, 2013). Several such studies have found that perinatally infected adolescents are more likely to have advanced HIV disease and a history of opportunistic infections, comorbidities, and additional physical and mental health problems than those who contracted HIV during adolescence (Pettitt, et al., 2013). This contributes to an increased risk for treatment failure and subsequent mortality for adolescents born with HIV, and makes their treatment more complicated than that of horizontally infected adolescents (Slogrove & Sohn, 2018).

Because perinatally infected ALHIV often initiate ART at a young age or even at birth, they are more likely to encounter treatment failure as they face a lifetime of ART use, including a limited range of approved drug regimens for pediatric formulations. In an analysis of a cohort of perinatally infected ALHIV in Europe, a fifth of the patients developed triple-class failure, that is, virological failure to at least two NRTIs, one NNRTI, and one protease inhibitor, by eight years of ART (Castro, et al., 2011). Another cohort study in the United States (Wong, et al., 2012) showed that urban adolescents with perinatally acquired HIV had been exposed to a median of eight ARV drugs due to developing drug resistance and toxicity. In low-resource settings there are additional challenges in identifying treatment failure early and therefore many patients accumulate drug resistance mutations (Sohn & Hazra, 2013). Other clinical challenges include an array of mental health issues, including high rates of symptoms indicative of anxiety and major depression among a cohort of children in Kenya between six and eighteen years of age (Kamau, et al. 2012). It is noted that, particularly in low-resource settings, perinatally infected ALHIV often experience other risk factors for mental illness including chronic illness, loss of a parent, stigma, and poverty, and that psychiatric symptoms are likely multifactorial. Neurodevelopment issues, cardiovascular disease, metabolic complications, kidney disease, and low bone mass have been observed in adolescents with perinatal HIV, primarily in studies done in high-income countries (Mofenson & Cotton, 2013).

Clinical outcomes in all persons living with HIV are dependent on strict adherence to ART, which is uniquely challenging for adolescents who are undergoing intense physical and psychological changes. This period of decreased parental supervision and increased autonomy can result in feelings of invincibility and an increase in risk-taking behaviors (Betz, 2004). ALHIV in resource-rich and resource-limited settings report lower adherence rates than adults and younger children. In a sub-Saharan Africa cohort, the proportion of perinatally infected ALHIV with 100% adherence was 20.7% at 6 months after initiation, 14.3% at 12 months, and 6.6% at 24 months, compared with 40.5%, 27.9%, and 20.6% complete adherence among adults at each time point (Agwu & Fairlie, 2013). This study utilized pharmacy refills to measure adherence, rather than utilizing self-reported adherence which can be unreliable and produces highly variable estimates.

In a systematic literature review of challenges in the treatment and management of adolescents with perinatally acquired HIV, authors Agwu and Fairlie (2013) identified common barriers and facilitators to

ART adherence. Barriers to adherence experienced by ALHIV that have been identified through numerous qualitative and quantitative studies include high pill burden, unpleasant side-effects of their medications, forgetfulness, variable school schedules, and stress related to disclosure. Additionally, cognitive barriers resulting from inadequate knowledge of HIV and the importance of ART adherence are common. Perinatally infected ALHIV are more likely to have experienced the loss of a parent or primary caregiver, or have a parent that is often ill, leading to additional stressors with possible negative impacts on adherence. ALHIV in resource-limited settings more often experience barriers resulting from high prevalence of comorbidities such as tuberculosis and malaria, as well as structural issues including housing instability, lack of transportation, or inadequate access to medical care, all of which can lead to nonadherence (Agwu & Fairlie, 2013).

Several protective factors have been identified specific to adolescents with HIV that was perinatally acquired, including in a mixed-methods study conducted in Kenya (Gitahi, et al., 2020). Researchers conducted focus group discussions and in-depth interviews with perinatally infected adolescents, collected sociodemographic data, and utilized medical record abstraction to identify common themes in the experiences and expectations of participants. They found that those who experienced earlier and complete disclosure had more positive outcomes than those with later or incomplete disclosure experiences. Participants identified having a parent or sibling with a similar HIV status as a source of support, a factor often unique to perinatally infected individuals. Additionally, participants reporting peer support among other ALHIV experienced better outcomes. Although research is advancing our understanding of the psychosocial needs of perinatally infected ALHIV, considerable gaps remain that would enable improvements in treatment and programming in limited-resource settings.

2.4 Predictors of adherence and clinical outcomes in adolescents living with perinatally acquired HIV

Factors impacting adherence to ART and subsequent health outcomes among ALHIV have been well documented, including in several studies done in sub-Saharan Africa. One such study conducted in Nairobi, Kenya aimed to determine factors that affect ART adherence among older, perinatally infected ALHIV. The data was collected through a cross-sectional study utilizing a structured, computer-assisted self-interviewing survey and medical chart abstraction. Researchers concluded that self-efficacy for HIV management and reduced pill burden were associated with increased adherence and viral suppression, and suggested that interventions designed to increasing self-efficacy be considered for adolescents transitioning to adult care (Gitahi, et al., 2020).

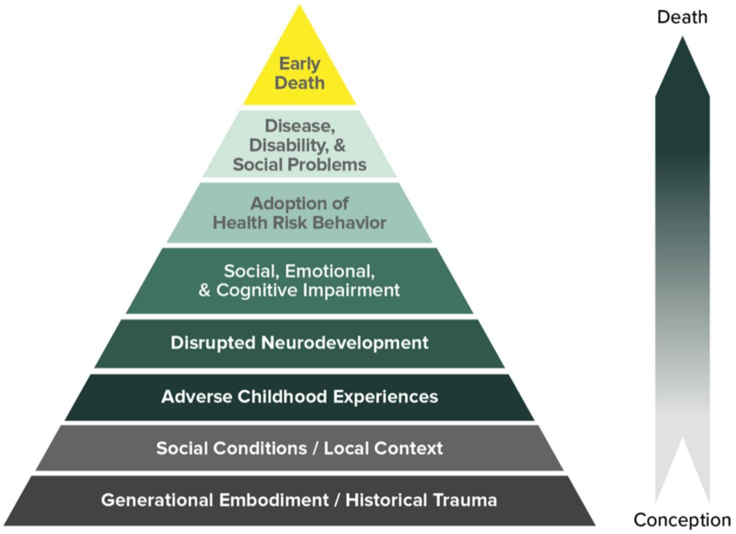
Similarly, the European and Developing Countries Clinical Trials Partnership Resistance Evolution Among Adolescents in Yaounde (EDCTP-READY) study conducted in Cameroon utilized a cross-sectional and analytical study design to determine factors associated with virological failure and drug resistance among perinatally infected ALHIV in both urban and rural settings. The outcomes measured were immunological failure, ARV drug resistance, and viral genetic diversity among the adolescents. Chi-square tests, Fisher's exact tests, multivariate logistic regression models, and linear regression models were used to determine associations between variables. Researchers Fokam, et al (2021) concluded that late adolescent age, female gender, and poor adherence were associated with poor virological and immunological outcomes in both rural and urban settings. A similar study done in the United States showed that incident stressful events (measured using a modified version of the Life Events Survey) were associated with non-adherence and virological failure among PLHIV, although this research was not specific to adolescents (Mugavero, et al., 2013).

Another negative outcome commonly used in research concerning ALHIV is loss to follow-up (LTFU). LTFU occurs when an individual is absent from the HIV treatment clinic for more than four months.

Research done in Kisumu, Kenya, found that factors associated with LTFU among ALHIV included pregnancy, a CD4 count above 350, and non-disclosure of ART status. Age, marital status, employment, WHO clinical disease stage, and education level were not significantly associated with LTFU in this study. The authors note that further research is needed to determine the reasons for LTFU and the true treatment outcomes of these ALHIV (Ojwang, et al., 2017).

2.5 Childhood adversities and HIV outcomes

There is a growing body of research attempting to understand the relationship between ACEs and health outcomes, however much of this research has focused on high resource settings such as the United States. In a review of childhood adversities and trauma, Oral et al. (2016) define ACEs and present epidemiologic data concerning these events and their health impacts. The largest study that has been conducted concerning ACEs and health later in life (known as The ACE Study) was done at Kaiser Permanente from 1995 to 1997 and found that childhood adversities are strongly correlated with developing risk factors for disease, as well as well-being later in life (*About the CDC-Kaiser ACE Study*, 2021). The ACE Study utilized the following conceptual framework to represent the mechanism for this relationship:



Mechanism by which Adverse Childhood Experiences
Influence Health and Well-being Throughout the Lifespan

ACEs fall into three categories: abuse, household challenges, and neglect. Each category then includes further subcategories, for a total of ten ACE classifications. These include household incidences of emotional, physical, and sexual abuse, violence, substance abuse, mental illness, parental separation, incarceration, and emotional or physical neglect. The original study showed that ACEs are quite common, with nearly two-thirds of participants reporting one or more ACE before the age of 18. Additionally, the research found a graded-dose response relationship between ACE score (the total sum of ACE categories reported) and negative outcomes (*About the CDC-Kaiser ACE Study*, 2021). Subsequent studies have found similar findings across a variety of settings, showing repeatedly that ACEs are a predictor of higher risk for poor health outcomes. These negative outcomes can be divided into four groups: (i) health risk behaviors, (ii) death and chronic health problems, (iii) poor mental health, and (iv) other outcomes. ACE research continues across populations, leading to further strategies in primary, secondary, and tertiary prevention (Oral, et al., 2016). Although most of this research has taken place in high-income countries, there a few notable exceptions in low-income settings in sub-Saharan Africa that are relevant to this thesis.

Psychological distress, often associated with adverse childhood experiences, has been shown to be correlated with poor adherence among adolescents in high and low-resource settings, including in a cross-sectional study done in Uganda (Mutumba, et al., 2016). This study showed an association between self-reported non-adherence and psychological distress levels, which were measured using a locally developed and validated five-point symptom checklist. Researchers also considered the role of psychosocial supports as mitigating factors to promote adherence, however found no significant associations. They conclude that further research is needed to investigate the impact of psychological distress among ALHIV in order to identify resources that could prevent the distress or mitigate its impact on adherence and subsequent virological outcomes. In another study done in rural Uganda, researchers Ashaba, et al. (2021) found that childhood trauma was significantly associated with major depressive disorder and suicidality. They also concluded that social support mitigates these effects of childhood trauma for depression, but not for suicidality. The authors note that a limitation exists due to the widespread use of corporal punishment in schools and homes as discipline, perhaps biasing the reporting of physical abuse.

In a review discussing the challenges faced by adolescents with perinatally acquired HIV in sub-Saharan Africa (Lowenthal, et al., 2014), this population is identified as having an increased likelihood of experiencing orphanhood, poverty, death of a sibling, or severe illness of a family member, all of which are considered adverse childhood experiences. The review identifies poor outcomes associated with these adversities, including increased risk taking, poor mental health, psychological distress, and inconsistent care. The authors highlight the need for more research to support prevention and mitigation strategies for those adverse experiences.

A study done in South Africa by researchers Kidman et al. (2018) sought to examine the relationship between childhood adversity and risky behaviors, but researchers also measured the association with virologic failure. Through their survey of 250 perinatally infected ALHIV, they found that half of their sample had experienced eight or more adversities, with the most common being emotional abuse, physical abuse, and witnessing domestic violence. There was a significant ($p < 0.01$) relationship between cumulative ACEs and behavioral risk-taking, with each ACE raising the odds of risky sexual behavior by about 30%. There was no significant relationship found between childhood adversity and viral suppression, although suppression was poor overall within the sample. ACEs were also associated with depression and substance abuse. They concluded that the risk of onward transmission of HIV was significant among perinatally infected ALHIV who have experienced childhood adversities.

2.6 Conclusion

Several conclusions can be drawn from the literature review above. Firstly, despite ALHIV in low-income settings bearing a large burden of the HIV epidemic, there are significant gaps in research concerning this population, and much of the existing research is not specific to perinatally infected adolescents. Adolescents living with HIV, and in particular those with perinatally acquired HIV, experience high rates of childhood adversity that impact their engagement in care and subsequent health outcomes. The few existing studies in low-income settings focus on a subset of ACEs, such as exposure to violence or experiencing orphanhood, and primarily show correlations with mental health or behavioral outcomes. Additionally, no studies were found utilizing qualitative data or a mixed-methods approach investigating the impacts of ACEs in sub-Saharan Africa. There exists a need to identify the relationship between ACEs and clinical outcomes among perinatally infected ALHIV in low-income settings, in order to develop prevention strategies and improve their quality of care.

Chapter III: Manuscript

Abstract

Background: Globally, adolescents living with HIV (ALHIV) bear a disproportionate burden of the HIV epidemic and this disparity is more pronounced in low-resource settings. In addition to increased risk of poor health outcomes, ALHIV are also more likely to experience adverse childhood experiences (ACEs). ACEs have been shown to have negative impacts on mental and physical health. Given the growing population of ALHIV, there is a need to better understand their challenges and lived experiences of this population, including ACEs and their impact on HIV care.

Objective: This study aimed to understand the effects of ACEs on the health of perinatally infected ALHIV, from the perspective of adolescents, caregivers, and providers; explore the relationship between ACEs and virological outcomes among ALHIV; and explore strategies that foster resilience among ALHIV following adversity, including the mitigating role of social support.

Methods: 130 randomly selected ALHIV engaged in care at study sites in Western Kenya participated in a survey. Purposive sampling was used to select 45 of these adolescents for focus groups (FGDs) (n=30) or in-depth interviews (IDIs) (n=15). Ten caregivers to ALHIV and 15 healthcare providers were recruited for additional interviews. Descriptive statistics and tests of association were used to assess relationships between ACEs and clinical outcomes; thematic analysis was used to identify recurring themes in the FGD and IDI data.

Results: The prevalence of ACEs was high, with a mean of 1.2 (SD=1.8) ACEs experienced by ALHIV. Several ACEs were significantly associated with poorer virological or clinical outcomes, and results varied by gender. A number of themes emerged from the qualitative findings, in which all participant types spoke of ALHIV experiences with abuse, neglect, and household challenges, and potential mitigators were proposed based upon personal experiences or observations.

Conclusions: Findings suggests that ACEs may negatively impact the later clinical outcomes of adolescents living with perinatally acquired HIV. Additional research is necessary in order to elucidate the pathways between ACEs and negative health outcomes in this population, and to further inform programs and policies to prevent ACEs and reduce their impact on engagement in care and the health and well-being of ALHIV.

Introduction

Adolescents aged 10-19 years are among the populations most severely impacted by the HIV epidemic, accounting for an estimated 2.1 million infections globally (Armstrong, et al., 2018). Eighty-four percent of adolescents living with HIV (ALHIV) live in sub-Saharan Africa, and this same population accounts for 90% of all ALHIV deaths (Slogrove & Sohn, 2018). With an estimated 130,000 ALHIV and 18,000 new infections in this age group each year, Kenya contributes significantly to the global burden of HIV among adolescents. Within the country, HIV remains the leading cause of death for adolescents and young people. Globally, ALHIV face unique challenges managing their illness during the complex transitional period of adolescence, and Kenyan ALHIV are more likely to be lost to follow-up, demonstrate poorer adherence to antiretroviral therapies, and have lower rates of viral suppression than other age groups (Luseno et al., 2017). Despite a lack of research differentiating outcomes of adolescents with perinatally acquired versus behaviorally acquired infections, it has been shown that those with perinatally acquired HIV are more likely to encounter treatment failure than those who acquire HIV during adolescence, as they initiate antiretroviral therapy (ART) at a young age and face a lifetime of ART use. In low-resource settings, ALHIV with perinatal infections often experience additional risk factors for mental and physical health complications including chronic illness, loss of a parent, stigma, and poverty (Mofenson & Cotton, 2013).

Adverse childhood experiences (ACEs) are potentially traumatic experiences that occur in childhood and fall into three categories: abuse, neglect, and household challenges. ACEs have been shown to be highly correlated with negative health outcomes later in life (Oral et al., 2016), and a graded-dose response association between ACE scores (a sum of ACE categories reported) and negative outcomes has been identified (*About the CDC-Kaiser ACE Study*, 2021). Among ALHIV in sub-Saharan Africa, there is a significant relationship between ACEs and behavioral risk, depression, and substance abuse (Kidman et al., 2018).

There is a paucity of data concerning ACEs and their impact on ALHIV in low-resource settings and in sub-Saharan Africa. Exploring this relationship is critical in order to improve engagement and retention in care and further develop trauma-informed care models for ALHIV. In this study we sought to understand the relationship between ACEs and adolescents' experience with HIV management and clinical outcomes among adolescents living with perinatally acquired HIV accessing outpatient treatment in Western Kenya.

Methods

Research Design

The study utilized a mixed-methods approach. Cross-sectional health related quality of life (HR-QOL) surveys which included adverse childhood experience screening questions were administered to participants to quantify the needs and experiences of ALHIV, and clinical and laboratory data was abstracted from participants' medical records. Qualitative methods (i.e. focus group discussions and in-depth interviews) were used to explore adolescents' experiences with HIV and to identify barriers to engagement in care. Qualitative methods were also used to explore these topics from the perspectives of caregivers and healthcare providers of participating ALHIV. Caregivers participated in in-depth interviews and focus groups, and providers participated in in-depth interviews.

Population and Sample:

The study population was made up of adolescents ages 11-19 years with perinatally acquired HIV infection in Kisumu and Homabay counties, Kenya. Inclusion for this study was limited to adolescents ages 11-19 years with documented or reported HIV infection at birth who were aware of their HIV status and currently receiving antiretroviral treatment. Also included were the caregivers and healthcare providers of eligible ALHIV.

The sample size for the quantitative survey was calculated based on a mother-to-child transmission rate of 8.3% in Kenya, a confidence interval of 95%, and an expected refusal rate of 10%. The sample size was determined to be 130 adolescents.

Procedures

ALHIV were recruited from Ministry of Health comprehensive care centers or HIV youth care centers in Kisumu and Homabay Counties that are funded by The U.S. President's Emergency Plan for AIDS Relief (PEPFAR). A systematic random sampling technique was utilized to recruit 130 ALHIV from study sites.

Adolescents were randomly selected during their weekly peer support groups from a participant roster and then screened for eligibility. During the screening visit participants aged 18 or over provided informed consent; where the participant was under 18, their guardian provided consent and the participant provided assent. Those who screened successfully for the study returned for an enrollment visit.

During the enrollment visit the informed consent/assent was reviewed. Demographic information was obtained, and a physical exam was performed. Relevant clinical and laboratory data, including recent viral load and CD4 count, current ART regimens, and vaccination record were abstracted from the medical record and if information was not available, blood samples were taken from participants and tests were ordered.

All 130 participants were given the HR-QOL survey to complete using a standardized digital platform. From the 130 eligible participants, 30 ALHIV were recruited for focus group discussions. Purposive sampling was used to select an additional 15 ALHIV for in-depth interviews**.** Caregivers of ALHIV (n=10) and providers (n=15) were also chosen to participate through purposive sampling. The interviews and focus groups were conducted in private locations to optimize participant comfort and the interviewers and moderators had training in social science and health research. The participants were given the choice to participate in the language in which they felt comfortable, including Swahili, Luo, and English. The interviews and focus groups were recorded, transcribed, and translated into English using a meaning-based approach (Esposito, 2001). The transcripts were deidentified and records containing identifiable information were kept in a secure location.

Instruments

The researchers used structured focus group discussion and interview guides to elicit information about the adolescents' lived experience, including their childhood experiences, family dynamics, sources of social support, relationships, disclosure experiences, experiences with school, mental health, barriers to engagement in care and challenges with adherence, facilitators to engagement, and unmet needs in their HIV care. The focus groups utilized a semi-structured discussion guide that aimed to support a focused intent with analytic comparability, while encouraging participants to respond freely. The in-depth interview guides were loosely structured with open-ended questions that allowed for variation in response and permitted the interviewer or respondent to introduce topics as appropriate. Key informant interview guides were developed to meet the same objectives from the perspectives of healthcare providers and caregivers of the participating adolescents.

The quantitative HR-QOL survey included demographic, socioeconomic, and health-seeking items in addition to questions specific to knowledge, attitudes, and practices of HIV care-seeking and treatment. The HR-QOL survey was adapted from the validated Rasch KIDSCREEN 27 survey (Ravens-Sieberer et al., 2007). KIDSCREEN 27 is a 27-item instrument used to assess the frequency of behaviors and feelings and their intensity, using five-point Likert scales. The survey targets five dimensions: physical wellbeing, psychological wellbeing, autonomy and parent relations, social support and peers, and school environment. Questions from this survey were adapted for the study's context, and supplemented with demographic questions, the HIV Stigma Scale of Berger et al. (2001), and the Adverse Childhood Experiences study questionnaire (Felitti, 2019). The HIV Stigma Scale is a 40-item instrument used to measure the perceived stigma of PLHIV using four-point Likert scales ranging from “strongly agree” to “strongly disagree”. The Adverse Childhood Experiences study questionnaire includes ten questions and is a widely used and validated tool used to determine the impact of abuse and neglect in childhood upon health later in life.

Analysis

The transcripts from the qualitative interviews and focus group discussions were analyzed using MaxQDA 2020 qualitative data analysis software (VERBI Software, 2020). Descriptive codes were developed inductively and deductively, creating a codebook through an iterative process using a sample of transcripts. The codebook included a description of each code, inclusion and exclusion criteria, and a quote representing a coded text example. The codes were then applied systematically to each transcript, using a partner coding approach to ensure the codes were applied reliably and consistently. A thematic analysis was conducted to identify and examine recurring themes, and themes were compared across groups.

Quantitative survey data and medical record abstraction data were analyzed using SAS statistical software version 9.4 (Cary, North Carolina). Composite ACE scores were calculated by totaling the number of ACEs reported by a respondent. Composite ACE scores were then transformed into categorical variables to denote low, medium, and high ACE levels. A low ACE level was defined as a composite score of zero to one ACE; a medium ACE level was defined as a composite score of two to three ACEs; and a high ACE level was defined as a composite score of 4 or more ACEs. Descriptive statistics were calculated for participant characteristics, including medical data and history of ACEs. Clinical outcomes, viral load, BMI, virological failure, and being on a second-line regimen of ART, were analyzed through comparison across history of individual ACEs and overall ACE score. Chi-squared tests of association were performed to determine associations between history of individual ACEs and categorical outcomes (virological failure and second-line regimen) and independent samples t-tests were used to identify relationships with continuous outcomes (viral load and BMI). One-way ANOVA tests were used to determine associations between ACE levels and clinical outcomes for continuous variables, and chi-squared tests of association were used to determine associations between ACE levels and clinical outcomes for categorical variables. All tests utilized a p-value of 0.05 to determine significance. All tests of association were calculated using both the full quantitative sample and stratified by gender.

Ethical Considerations

The study was approved by the Kenya Medical Research Institute (KEMRI) Scientific and Ethics Review Unit and the Institution Ethics Review Board of Jaramogi Oginga Odinga Referral Hospital (JOOTRH). Study protocol, informed consent forms, and instruments were submitted for approval. Privacy and confidentiality were prioritized consistent with guidelines for research involving young people. Participants provided written informed consent and those who were still minors at the time of enrollment provided assent and their parent or guardian provided consent. The present sub-study was the secondary analysis of deidentified data provided by KEMRI, hence did not require Emory IRB approval.

Results

Characteristics of ALHIV Sample

Sixty-seven (51.1%) of the adolescents in the quantitative sample were male and 64 (48.9%) were female (**Table 1**). The average age was 14.6 years old, with a range of 11 to 19 years and a standard deviation of 2.4 years. The average age at diagnosis was 5.1 years (SD=3.8). The majority of participants' HIV infections were classified as WHO stages II or III (35.0% each, n=46), with 22.9% (n=29) in WHO stage I at the time of enrollment and a small portion (6.9%, n=9) presenting with the most advanced stage of disease progression, WHO stage IV. The average BMI was 18.1 kg/m^2 with a standard deviation of 3.1 kg/m^2. The average viral load, as measured at study enrollment, was 5,637.8 copies/mm^3 with a standard deviation of 31,285.4 copies/mm^3. Forty-six adolescents (35.1%) had undetectable viral loads and the majority of participants (74.0%, n=97) were virally suppressed at enrollment (viral load less than 1,000 copies/mm^3). Thirty-eight participants (29.0%) had experienced treatment failure and were on second line regimens. The characteristics of the qualitative sample were similar, with the exception of average age at diagnosis, which was 7.6 years. There were purposive sampling techniques used to select older and more expressive adolescents for interviews, and the older age at diagnosis for this sample may point to a relationship between age at diagnosis and current engagement in care.

Prevalence of ACEs

A summary of the ACE survey results is shown in **Table 2**. Sixty-six (50.4%) of the adolescents reported having experienced no ACE and 65 (49.7%) reported having had one or more ACEs. The average number of adversities reported was 1.2 (SD=1.8). The most commonly reported ACE was physical abuse, with 31 adolescents (23.7%) reporting having experienced physical abuse by a parent or caregiver. ACE scores were not associated with gender, and male and female adolescents reported each ACE with similar frequencies, with the exception of witnessing domestic violence which was more commonly experienced by females (14.1%, n=9) than males (3.0%, n=2).

Effects of ACEs

Overall

An increasing level of ACE score was significantly associated (p=0.03) with virological failure, but no other clinical outcomes showed significant associations with increasing ACE score. Associations between ACE score and clinical outcomes are shown in **Table 3**. A number of ACEs were independently associated with clinical outcomes as shown in **Tables 4-7** and described below.

A number of themes emerged from the qualitative findings, in which ALHIV, caregivers, and providers spoke of three main categories of childhood adversities and their implications for adolescents' engagement in care. Abuse, neglect, and household challenges were discussed by all three informant types, and potential mitigators were proposed based upon personal experiences or observations.

Abuse

Abuse encompasses verbal, physical, and sexual forms of abuse. One or more types of abuse were reported to have been experienced by 29.2% (n=38) of the adolescents in the quantitative sample. The association between experience of verbal abuse and higher viral load was significant (p=0.01). Seven (5.3%) adolescents reported having experienced sexual abuse in the survey, and this showed a significant association (p=0.01) with higher viral load among female participants (**Table 6)**.

Those interviewed shared experiences with physical and verbal abuse from caregivers, other family members, teachers, and other adults in their communities. Adolescents commonly attributed the abuse to their HIV status and cited abuse as a barrier to drug adherence and/or engagement in care. Among these qualitative findings, abuse seemed to be associated with partial or complete orphanhood, with the perpetrator of the abuse often being a stepparent or other non-parent caregiver. One adolescent who was living with her older sister described an experience of physical abuse by her brother-in-law:

> *"He didn't want anything to do with HIV. So when he found my drugs…you know you cannot hide something in someone's house…there was a time he used to beat me. As in as if he didn't want me."* *– Adolescent female, focus group discussion*

In key informant interviews, providers spoke on abuse more broadly and often made direct links to impacts on internalized stigma, mental health, and engagement in care. They often cited orphanhood as a common cooccurrence with abuse, especially if a child is living with a discordant status caregiver. When asked about challenges in caring for ALHIV, one provider cited abuse as a main challenge:

> *"And another thing you get that maybe it's a partial orphan may be a mother has died, the father has married another wife and the child is being mistreated at home and because of the mistreatment he gives up and when he comes here he is very sad, he wants somebody to support, you cannot support because he is not getting the care and the support that he needs from home"* *– Provider, in-depth interview*

Although personal experiences of sexual abuse were not recounted by any adolescents during in-depth interviews or focus groups, some participants shared that this was a challenge faced by ALHIV more generally. Caregivers, providers, and adolescents believed that ALHIV were more vulnerable to experiencing sexual abuse due to HIV-related stigma, both enacted stigma from abusers who target ALHIV and internalized stigma contributing to low self-worth among ALHIV. Additionally, informants believed that financial need, often exacerbated by HIV infection, could increase the risk of sexual abuse as well. One participant shared that sexual abuse is a common challenge among ALHIV in his community:

> ***"I: So is there anything regarding experiences and challenges adolescents living with HIV face in the community that we did not talk about today but you think is important to include?***
>
> *R: Yeah like mistreatment.*
>
> ***I: Mistreatment how? Can you explain?***
>
> *R: Like people in the community sexually abusing them.*
>
> ***I: In sexual abuses?***
>
> *R: Yeah. They see you as less important so they can use you however they want."*
>
> *– Adolescent male, age 17, in-depth interview*

Neglect

Although 19.8% (n=26) of the ALHIV in the quantitative sample reported experiencing neglect, there were no significant associations between either physical or emotional neglect and clinical outcomes among the full sample. When stratified by gender, however, a significant association (p<0.01) emerged between emotional neglect and lower BMI among male adolescents (**Table 6**).

Among the qualitative sample the most commonly discussed ACE within the interviews was neglect, or the ongoing failure to meet a child's basic needs, emotionally or physically. All informant types believed neglect to be a significant barrier to adherence, often citing inadequate provision of food as a reason for missed doses of ART and subsequent rises in viral load. Several (n=3) caregivers interviewed who were not biological parents had become the primary caregivers of the ALHIV due to parental neglect specific to their HIV care (i.e. failing to provide medication, adequate food, or otherwise meet healthcare needs). One adolescent described the experience of shifting caregivers due to neglect:

> ***"I: You have told me that you stay with your aunt and she is the one giving you drugs. How was your relationship with this family while you were taking your drugs?***
>
> *R: My mother died when I was young and I was staying with my father. So I can't know because my father was not taking part in his responsibility well and even lost my older sister. So my mother's sister took me to stay with her."*
>
> *– Adolescent male, age 14, in-depth interview*

All providers recalled experiences when neglect, both physical and emotional, made treating ALHIV challenging. Few (n=3) adolescents described instances of emotional neglect, but in each case this was attributed to their HIV status. Physical neglect described by the adolescents was most often attributed to the inadequate provision of food as this related to their ART adherence. One provider described the challenge of caring for adolescents experiencing neglect:

> *"We have those who stay in the family, they are not rejected clearly but you can see they are left alone to die. We have such cases, where they are left alone. They have no one to remind them that they need to take their medicine and they have nobody to support them when they want to come to the clinic and even when you want somebody to come on board to help them, you find that there is such a big family yes but they are all scattered around these children. There is nobody to bring on board squarely and say this is the person we want to be a treatment supporter to this child. To me I just say that these children have been left alone to die."*
>
> *– Provider, in-depth interview*

Household challenges

Among the ALHIV who completed the survey, 27.5% (n=36) reported having experienced an ACE relating to one or more household challenge, which includes losing a parent due to death or divorce, witnessing domestic violence, having a family member who abuses alcohol or drugs, having a family member with a mental illness, or having a family member go to prison. Witnessing domestic violence was reported by 11 (8.4%) adolescents and showed a significant association (p=0.02) with higher viral load (**Table 6**). In contrast, both having a family member who abuses alcohol or drugs (p=0.03) and having a family member with mental illness (p<0.001) had significant protective associations with a lower viral load. When stratified by gender, having a family member go to prison shows a significant protective association (p=0.05) with higher BMI among female adolescents.

The loss of a parent was frequently recounted by ALHIV and often cited as a barrier to engagement in care, as well a factor contributing to additional ACEs. Providers also found the loss of a parent to be a challenge in caring for ALHIV, and noted that this was distinctive to perinatally acquired infections, occurring less frequently among adolescents with behaviorally acquired HIV.

> *"The adolescents have challenges sometimes may be they are total orphans and the care givers are being changed from one care giver to another that is the highest challenge that we have and because of that now we get many adolescents failing in their treatment, the viral load goes high and following them becomes a problem"* *– Provider, in depth interview*

In the qualitative data, no ALHIV described family members with alcoholism or drug misuse, despite 13.7% of the survey respondents reporting having experienced this ACE. However, providers described the challenge of caring for ALHIV with a parent who is an alcoholic and the poor adherence that resulted from decreased supervision. Witnessing domestic violence and mental illness were not described by informants during interviews or focus groups.

Potential mitigators

Although the quantitative analysis did not provide insight into mitigating factors, the qualitative data provided a few insights into factors that may mitigate the harms of ACEs. Many informants mentioned a parent with shared HIV status as a potential mitigator to childhood adversities, due to the shared understanding of a lived experience and the unique physical and emotional needs of PLHIV. Additionally, having siblings with a shared status was discussed as a facilitator to ART adherence. ALHIV identified the utilization of community resources, such as clinic-based support groups, as a coping mechanism and source of social support outside of their families.

Discussion

To the best of our knowledge, this study is the first to first to consider the relationship between adverse childhood experiences (ACEs) and clinical outcomes among adolescents living with perinatally acquired HIV in sub-Saharan Africa. Perinatally acquired HIV places adolescents at an increased risk of poor outcomes because these individuals often undergo a lifetime of ART use, resulting in a higher likelihood of treatment failure (Pettitt, et al., 2013). Furthermore, adolescents with perinatally acquired HIV are more likely to lack social support, as one or both parents are more likely to be lost or experience severe illness due to their own HIV (Mofenson & Cotton, 2013). Our qualitative and quantitative analyses suggest that ACEs may negatively impact virological and other clinical outcomes within this population. Our findings are consistent with similar studies done in high-resource settings (Kacanek, et al., 2016), and contribute to the growing body of evidence showing that ACEs negatively impact later-in-life health outcomes (Oral, et al., 2016).

In agreement with other studies on ACEs among PLHIV, the adolescents in our sample reported more ACEs than are expected in the general population (LeGrand, et al., 2016). Females and males reported similar rates of ACEs, with the exception of witnessing domestic violence, which was reported by nearly five times as many females as males. This may point to a difference in how female and male adolescents perceive domestic violence and the topic warrants further investigation. An increasing ACE level was significantly associated with virological failure, but the associations between ACE level and other clinical outcomes were not statistically significant . Several ACEs were independently associated with poor clinical outcomes, including higher viral load and lower BMI. The qualitative findings provide some insight into the mechanisms by which ACEs negatively impact the health of the ALHIV, however much remains unknown about these pathways.

Among the three types of abuse (physical, verbal, and sexual), physical abuse was the most commonly reported. This is unsurprising, as the practice of corporal punishment is common in Kenya (Ministry of Labour and Social Protection of Kenya, 2019). Qualitative findings suggest that orphanhood is related to the experience of abuse, both physical and verbal. This is consistent with findings from larger studies showing that children who experience AIDS-related orphanhood are at an increased risk for abuse (Sharp, et al., 2016). Verbal abuse was also common among study participants and the qualitative data suggests that much of this verbal abuse was related or attributed to an individual's HIV status. This finding is consistent with that of studies on enacted stigma in low-resource settings, often taking the form of verbal abuse targeting PLHIV (Dlamini, et al., 2007). Among study participants, verbal abuse was significantly associated with an increased viral load. Previous research has shown that enacted and internalized stigma caused by verbal abuses can reduce an individual's engagement in HIV management, often as the result of concealment efforts made by the individual to hide their HIV status from potential abusers (Akatukwasa, et al., 2021). The perspective of healthcare providers in our qualitative findings supports a similar pathway.

Sexual abuse showed a significant association with higher viral load among only female ALHIV in this study. This finding is likely linked to females being at a higher risk of experiencing sexual abuse compared to their male counterparts (Richter, et al., 2015). Additionally, sexual abuse is consistently under-reported across various populations and settings and therefore the effect in male ALHIV may be an under-estimate (Cluver, et al., 2019). It has been proven that sexual abuse interferes with an individual's development of general self-efficacy and can increase shame and isolation (Richter, et al., 2015). Self-efficacy is vital to maintaining engagement in HIV care, especially for older adolescents gaining independence and managing their illness without direct supervision of a caregiver.

Physical neglect showed no significant association with virological or clinical outcomes and was reported by fewer adolescents compared to physical or verbal abuse. This was inconsistent with the qualitative findings, in which all informant types described physical neglect as one of the greatest challenges to ART adherence. Caregivers, providers, and ALHIV all believe that inadequate provision of food is a significant barrier to taking ART medications consistently and shared personal experiences or observations of this. This therefore suggests that physical neglect was underreported, perhaps because ALHIV attribute the lack of food to circumstances outside their household’s control.

The most commonly reported household challenges included having a parent who misused alcohol or drugs, or having a parent who was imprisoned. By contrast, neither of these ACEs were mentioned by ALHIV in the qualitative interviews or focus groups. One possible reason may be that these topics are sensitive and less likely to be discussed openly. Another may be that these experiences do not significantly impact engagement in care, which can be supported by the quantitative findings that imply a protective relationship between these ACEs and clinical outcomes.

A major strength of this study is in the mixed-methods design, by which perspectives on challenges, coping strategies, and potential mitigators were gained from three informant types. One incidental finding was the suggestion that having a parent or a sibling with shared HIV status may mitigate the negative effects on clinical outcomes. Further investigation is needed to explore this, as it remains unclear if this protective effect acts as primary prevention of childhood adversities, or a later mitigator allowing continued engagement in care and facilitating adherence to ART regimens despite past or ongoing trauma.

There are several limitations to this study. The first, as mentioned above, is that the common practice of corporal punishment makes it difficult to interpret the results concerning physical abuse. Secondly, the variables viral load and BMI had differing amounts of missing data, 6.9% and 27.7%, respectively. ALHIV with missing values for these variables were not included in the corresponding association tests and therefore their reported ACEs were omitted from those tests as well, reducing the effective sample size for those calculations. A third limitation is the small sample size. Although some associations were significant, larger samples are needed to determine the risks of childhood adversities. Finally, the cross-sectional design of our study cannot determine the temporality of ACEs and declines in clinical outcomes.

In conclusion, our study suggests that experiencing adversity in childhood may negatively impact the later clinical outcomes of adolescents living with perinatally acquired HIV. As HIV treatment continues to improve and more children born with HIV survive into adolescence and adulthood, it is paramount that we further our understanding of this population’s unique challenges to HIV care and management. Further exploration is needed to determine the causal pathways from childhood adversities to reduced clinical outcomes. However, our findings suggest that screening for ACEs when ALHIV present for treatment could allow clinic staff to provide trauma-informed care. Additionally, providers would be able to refer adolescents to the social or psychological supports needed to ensure engagement in care is maintained and ALHIV transition successfully to adulthood and subsequent independent HIV management.

Chapter IV: Conclusion

Our research found through qualitative and quantitative analysis that ACEs may negatively impact virological and other clinical outcomes among adolescents with perinatally acquired HIV. Our results also suggest that the associations between ACEs and clinical outcomes may vary by gender, and that some ACEs are potentially protective. These findings have implications for where further research is needed as well as where new policies may need to be implemented.

Future research should be conducted in order to determine causal pathways between ACEs and clinical outcomes. Larger sample sizes are needed as well as a study design which can establish temporality between the exposures and outcomes. Additionally, a larger sample size would allow a dose-response relationship to be examined based on the cumulative effect of ACEs on various clinical outcomes. Although determining causation would require substantial and longitudinal quantitative data collection and analysis, our research also highlights the value of mixed-method study design. The perspectives gained from interviews and focus groups with several informant types gave insight into the lived of experience of ALHIV and those involved in their care. Continued research on ACEs among ALHIV should integrate qualitative components in order to collect and analyze valuable data and maintain community engagement in the field.

Our research can be used to inform policies for HIV clinics and treatment centers where adolescents seek care. These findings suggest that adolescents with perinatally acquired HIV face unique challenges that may not be shared with adolescents who acquire HIV horizontally, which is consistent with previous findings concerning this population (Mofenson & Cotton, 2013). Among these unique challenges is the increased risk of childhood adversities inhibiting engagement in HIV treatment and resulting in poorer clinical outcomes, supporting a need for ACE prevention.

Because of the complex inter-relatedness of the socio-political context, community, family, and individual contributing to the occurrence of child adversities, the socio-ecological model can provide a framework to conceptualize ACE prevention strategies. Programs and policies to prevent ACEs and reduce the negative impact they cause must occur on each level to produce the desired effect (Krug, et al., 2022). Primary, secondary, and tertiary prevention strategies should be enacted in order to combat the harmful effects of ACEs among this population.

Primary efforts, targeting the prevention of ACEs occurring, can be made when young children initially present for care or during PMTCT care during and following pregnancy. Those at risk for adversities can be assessed and given the necessary household social supports or connected with community-based organizations with the goal of preventing ACEs entirely. Currently, primary prevention efforts are rare in both high- and low-resource settings (Oral, et al., 2013). Secondary prevention, such as providing support immediately following an adversity in order to minimize the harmful effects, can be implemented by consistently screening for adversities as children and adolescents continue to present for care. Among ALHIV, secondary prevention strategies must include components that facilitate continued adherence to ART regimens in order to avoid virological failure or opportunistic infections. Tertiary prevention strategies can take the form of integrated psychological care including cognitive behavioral therapy in order to treat the long-term consequences of childhood adversities among adolescents. Both secondary and tertiary prevention strategies are included in trauma-informed care models, which have been proposed to reduce the long-term consequences of ACEs. These models attempt to build resilience and prevent re-traumatization when patients who have experienced ACEs present for care (Lacey & Minnis, 2019).

In conclusion, our research adds to the growing body of evidence supporting ACE prevention and trauma-informed care, while highlighting the unique challenges and needs of adolescents living with perinatally acquired HIV in low-resourced settings. Additional research is necessary in order to elucidate the pathways between ACEs and clinical outcomes in this population and to further inform programs and policies to prevent ACEs and reduce their impact on engagement in care and the health and well-being of ALHIV.

Tables

Table 1 Demographic and clinical characteristics of quantitative sample

Characteristic	Total	Females	Males
Gender, n (%)			
Male	67 (51.1)	-	-
Female	64 (48.9)	-	-
Age (years), mean (SD)	14 (2.4)	14.2 (2.3)	15.0 (2.4)
Age at diagnosis (years), mean (SD)	5.1 (3.8)	5.1 (3.5)	5.0 (4.0)
WHO Stage, n (%)			
I	29 (22.9)	12 (18.8)	18 (27.2)
II	46 (35.1)	29 (45.3)	17 (25.8)
III	46 (35.1)	21 (32.8)	24 (36.4)
IV	9 (6.9)	2 (3.1)	7 (10.6)
BMI (kg/m2), mean (SD)	18.1 (3.1)	18.3 (3.1)	17.9 (3.1)
Viral load (copies/ml), mean (SD)	5,637.8 (31,285.4)	5798.42 (6637.0)	5440.5 (11302.5)
Virological failure, n (%)	24 (19.8)	12 (20.3)	12 (19.4)
Second line regimen , n (%)	38 (29)	17 (26.6)	21 (31.8)

Table 2 Prevalence of ACEs among quantitative sample

ACE	Total n (%)	Females n (%)	Males n (%)
Physical abuse	30 (22.9)	14 (22.9)	16 (24.2)
Verbal abuse	18 (13.7)	7 (10.9)	11 (16.7)
Sexual abuse	7 (5.3)	3 (4.7)	4 (6.1)
Emotional neglect	14 (10.7)	7 (10.9)	7 (10.6)
Physical neglect	14 (10.7)	6 (9.4)	8 (12.1)
Losing a parent	14 (10.7)	9 (14.1)	5 (7.6)
Witnessing domestic violence	11 (8.4)	9 (14.1)	2 (3.0)
Alcoholism or drug use	18 (13.7)	8 (12.5)	10 (15.2)
Mental illness	8 (6.1)	5 (7.8)	3 (4.5)
Prison	20 (15.3)	8 (12.5)	12 (18.2)

Table 3 Associations between clinical outcomes and increasing ACE level as assessed using one-way ANOVA tests and chi-square tests of association

	F-value	P-value
Viral load	0.52	0.5981
BMI	1.19	0.3085

		Low (0-1)	Medium (2-3)	High (>4)	
Virological failure	Yes	15 (12.4)	8 (6.6)	1 (0.8)	0.0342
	No	73 (60.3)	12 (9.9)	12 (9.9)	
Second line regimen	Yes	29 (22.3)	8 (6.2)	1 (0.8)	0.1239
	No	66 (50.8)	13 (10)	13 (10)	

Table 4 ACEs associated with continuous clinical outcomes as assessed using independent samples t-tests

-		Viral load (copies/mL) mean (SD)	BMI (kg/m2) mean (SD)
Physical abuse	Yes (n=30)	3238 (10318)	18.2 (2.7)
	No (n=100)	2032 (4911)	18.04 (3.2)
	P-value	0.5516	0.7977
Verbal abuse	Yes (n=18)	3354 (10056)	17.9 (2.7)
	No (n=112)	709 (1736)	18.1 (3.2)
	P-value	0.0155	0.8997
Sexual abuse	Yes (n=7)	5722 (15115)	18.6 (1.0)
	No (n=123)	2761 (8900)	18.1 (3.2)
	P-value	0.6257	0.3961
Emotional neglect	Yes (n=14)	4044 (7500)	16.7 (2.4)
	No (n=116)	2787 (9531)	18.3 (3.1)
	P-value	0.5756	0.0661
Physical neglect	Yes (n=14)	1400 (3127)	18.4 (1.9)
	No (n=116)	3086 (9699)	18.1 (3.2)
	P-value	0.2102	0.6186
Losing a parent	Yes (n=14)	2488 (5480)	18.6 (3.8)
	No (n=116)	2990 (9706)	18.1 (3.02)
	P-value	0.775	0.6704
Witnessing domestic violence	Yes (n=11)	3146 (9673)	17.9 (3.1)
	No (n=119)	559 (1698)	19.7 (2.8)
	P-value	0.0172	0.1086
Alcoholism or drug use	Yes (n=18)	822 (2087)	19.0 (2.8)
	No (n=112)	3277 (9962)	18.0 (3.1)
	P-value	0.0276	0.2662
Mental illness	Yes (n=8)	31 (63)	17.6 (2.0)
	No (n=122)	3110 (9556)	18.1 (3.2)
	P-value	0.0008	0.5560
Prison	Yes (n=20)	1290 (2752)	18.8 (2.8)
	No (n=110)	3238 (10041)	18.0 (3.1)
	P-value	0.1011	0.2939

Table 5 ACEs associated with categorical clinical outcomes as assessed using chi-square tests of association

		Virological failure		Second line regimen	
		Yes	No	Yes	No
Physical abuse	Yes	5 (4.1)	23 (19.1)	8 (6.1)	22 (16.9)
	No	19 (15.7)	73 (60.3)	29 (22.3)	70 (53.8)
	P-value		0.7461		0.7805
Verbal abuse	Yes	2 (1.7)	16 (13.2)	3 (2.3)	15 (11.5)
	No	22 (19.0)	80 (66.1)	34 (26.2)	77 (59.2)
	P-value		0.3065		0.2243
Sexual abuse	Yes	1 (0.8)	6 (5.0)	1 (0.8)	6 (4.6)
	No	23 (19.0)	91 (75.2)	37 (28.5)	86 (66.2)
	P-value		0.7045		0.3714
Emotional neglect	Yes	5 (4.1)	9 (7.4)	2 (1.5)	12 (9.2)
	No	19 (15.7)	88 (72.7)	36 (27.7)	80 (61.5)
	P-value		0.1131		0.1931
Physical neglect	Yes	2 (1.7)	9 (7.4)	3 (2.3)	11 (8.5)
	No	22 (18.2)	88 (72.7)	35 (26.9)	81 (62.3)
	P-value		0.8854		0.4968
Losing a parent	Yes	4 (3.3)	10 (8.3)	1 (0.8)	10 (7.7)
	No	20 (16.5)	87 (71.9)	34 (26.2)	82 (63.1)
	P-value		0.3833		0.9542
Witnessing domestic violence	Yes	1 (0.8)	9 (7.4)	1 (0.8)	10 (7.7)
	No	23 (19.0)	88 (72.7)	37 (28.5)	82 (63.1)
	P-value		0.4155		0.1248
Alcoholism or drug use	Yes	3 (2.5)	14 (11.6)	2 (1.5)	16 (12.3)
	No	21 (17.4)	83 (68.6)	36 (27.7)	76 (58.5)
	P-value		0.8072		0.049
Mental illness	Yes	0 (0.0)	7 (5.8)	1 (0.8)	7 (5.4)
	No	24 (19.8)	90 (74.4)	37 (28.5)	85 (65.4)
	P-value		0.1751		0.2828
Prison	Yes	5 (4.1)	14 (11.6)	4 (3.1)	16 (12.3)
	No	19 (15.8)	83 (68.6)	34 (26.2)	76 (58.5)
	P-value		0.4403		0.9736

Table 6 ACEs associated with continuous clinical outcomes stratified by gender as assessed using independent samples t-tests

	Females			Males		
-		Viral load (copies/mL) mean(SD)	BMI (kg/m2) mean (SD)		Viral load (copies/mL) mean (SD)	BMI (kg/m2) mean (SD)
Physical abuse	Yes (n=14)	2659 (5824)	19.6 (3.1)	Yes (n=16)	1488 (4094)	16.9 (1.2)
	No (n=50)	2376 (6975)	18.0 (3.1)	No (n=51)	4064 (12754)	18.2 (3.4)
	P-value	0.8843	0.1535	P-value	0.2335	0.0683
Verbal abuse	Yes (n=7)	2652 (7080)	18.5 (1.9)	Yes (n=11)	4055 (12374)	17.6 (3.2)
	No (n=57)	894 (1985)	18.3 (3.2)	No (n=56)	4056 (12374)	17.9 (3.1)
	P-value	0.004	0.8133	P-value	0.0597	0.8684
Sexual abuse	Yes (n=3)	6252 (1791)	19.3 (0.7)	Yes (n=4)	10000 (20000)	17.9 (0.9)
	No (n=61)	2526 (6792)	18.3 (3.2)	No (n=63)	2988 (10603)	17.9 (3.2)
	P-value	0.0078	0.2205	P-value	0.5356	1.9627
Emotional neglect	Yes (n=7)	5209 (8214)	18.1 (2.2)	Yes (n=7)	2879 (7160)	15.0 (1.5)
	No (n=57)	2020 (6398)	18.4 (3.2)	No (n=60)	3512 (11771)	18.2 (3.1)
	P-value	0.3562)	0.8136	P-value	0.8438	0.0029
Physical neglect	Yes (n=6)	1504 (2872)	19.0 (1.6)	Yes (n=8)	1341 (3488)	17.9 (2.3)
	No (n=58)	2464 (6840)	18.3 (3.2)	No (n=59)	3708 (11929)	17.9 (3.2)
	P-value	0.5945	0.1974	P-value	0.2642	0.9607
Losing a parent	Yes (n=9)	3766 (6601)	19.6 (4.3)	Yes (n=5)	187 (393)	16.6 (1.9)
	No (n=55)	2152 (6680)	18.2 (3.0)	No (n=62)	3726 (11752)	18.0 (3.2)
	P-value	0.5139	0.4378	P-value	0.0277	0.3475
Witnessing domestic violence	Yes (n=9)	6991 (1896)	20.2 (3.0)	Yes (n=2)	11474 (1481)	18.0 (0.9))
	No (n=55)	2665 (7075)	18.0 (3.0)	No (n=65)	3555 (8179)	17.9 (3.2)
	P-value	0.1077	0.117	P-value	0.0196	0.9025
Alcoholism or drug use	Yes (n=8)	1086 (2968)	20.9 (3.0)	Yes (n=10)	587 (938)	17.3 (1.4)
	No (n=56)	2604 (7039)	18.0 (3.0)	No (n=57)	3925 (12169)	18.0 (3.3)
	P-value	0.3028	0.0647	P-value	0.0547	0.3959
Mental illness	Yes (n=5)	2513 (661)	17.4 (2.5)	Yes (n=3)	3615 (1505)	18.0 (0.9)
	No (n=59)	6846 (2568)	18.4 (3.2)	No (n=64)	11563 (6628)	17.9 (3.2)
	P-value	0.0088	0.5005	P-value	0.0195	0.9025
Prison	Yes (n=8)	1269 (2923)	21 (2.9)	Yes (n=12)	1205 (2768)	17.4 (1.6)
	No (n=56)	2576 (7047)	18.0 (3.0)	No (n=55)	3901 (12373)	18.0 (3.4)
	P-value	0.3701	0.0482	P-value	0.1821	0.4489

Table 7 5 ACEs associated with categorical clinical outcomes stratified by gender as assessed using chi-square tests of association

		Females				Males			
		Virological failure		Second line regimen		Virological failure		Second line regimen	
		Yes	No	Yes	No	Yes	No	Yes	No
Physical abuse	Yes	3 (5.2)	10 (17.2)	3 (4.8)	11 (17.5)	2 (3.2)	13 (21.0)	5 (7.6)	11 (16.7)
	No	9 (15.5)	36 (62.1)	13 (20.6)	36 (57.1)	10 (16.1)	37 (59.7)	16 (24.2)	34 (51.5)
	P-value		0.8094		0.6989		0.4978		0.9553
Verbal abuse	Yes	1 (1.7)	6 (10.3)	0 (0.0)	7 (11.1)	1 (1.6)	10 (16.1)	3 (4.5)	8 (12.1)
	No	11 (18.9)	40 (69.0)	16 (25.4)	40 (63.5)	11 (17.7)	40 (64.5)	18 (27.3)	37 (56.1)
	P-value		0.6556		0.1016		0.3421		0.7229
Sexual abuse	Yes	0 (0.0)	3 (5.2)	1 (1.6)	2 (3.2)	1 (1.6)	3 (4.8)	0 (0.0)	4 (6.1)
	No	12 (20.7)	44 (75.9)	16 (25.4)	45 (71.4)	11 (17.7)	47 (75.8)	21 (31.8)	41 (62.1)
	P-value		0.3690		0.7856		0.7676		0.1586
Emotional neglect	Yes	4 (6.9)	3 (5.2)	1 (1.6)	6 (9.5)	1 (1.6)	6 (9.7)	1 (1.5)	6 (9.1)
	No	8 (13.8)	44 (75.9)	16 (25.4)	41 (65.1)	11 (17.7)	44 (71.0)	20 (30.3)	39 (59.1)
	P-value		0.01		0.4358		0.7185		0.2922
Physical neglect	Yes	1 (1.7)	3 (5.2)	1 (1.6)	5 (7.9)	1 (1.6)	6 (9.7)	2 (3.0)	6 (9.1)
	No	11 (19.0)	44 (75.9)	16 (25.4)	42 (66.7)	11 (17.7)	44 (71.0)	19 (28.8)	39 (59.1)
	P-value		0.8104		0.5643		0.7185		0.6587
Losing a parent	Yes	4 (6.9)	5 (8.6)	3 (4.8)	6 (9.5)	0 (0.0)	5 (8.1)	1 (1.5)	4 (6.1)
	No	8 (13.8)	42 (72.4)	14 (22.2)	41 (65.1)	12 (19.4)	45 (72.5)	20 (30.3)	41 (62.1)
	P-value		0.051		0.6198		0.2533		0.5551
Witnessing domestic violence	Yes	1 (1.7)	7 (12.1)	1 (1.6)	8 (12.7)	0 (0.0)	2 (3.2)	0 (0.0)	2 (3.0)
	No	11 (19.0)	40 (69.0)	16 (25.4)	39 (61.9)	12 (19.4)	48 (77.4)	21 (31.8)	43 (65.2)
	P-value		0.5535		0.2576		0.4813		0.3266
Alcoholism or drug use	Yes	1 (1.7)	7 (12.1)	1 (1.6)	7 (11.1)	2 (3.2)	7 (11.3)	1 (1.5)	9 (13.6)
	No	11 (19.0)	40 (69.0)	16 (25.4)	40 (63.5)	10 (16.1)	43 (69.4)	20 (30.3)	36 (54.5)
	P-value		0.5535		0.3357		0.8138		0.1078
Mental illness	Yes	0 (0.0)	4 (6.9)	1 (1.6)	4 (6.3)	0 (0.0)	3 (4.8)	0 (0.0)	3 (4.5)
	No	12 (20.7)	43 (74.1)	16 (25.4)	43 (68.3)	12 (19.4)	47 (75.8)	21 (31.8)	42 (63.6)
	P-value		0.2952		0.7293		0.3844		0.2259
Prison	Yes	2 (3.4)	6 (10.3)	1 (1.6)	7 (11.1)	3 (4.8)	8 (12.9)	3 (4.5)	9 (13.6)
	No	10 (17.2)	41 (70.7)	16 (25.4)	40 (63.5)	9 (14.5)	42 (67.7)	18 (27.3)	36 (54.5)
	P-value		0.7246		0.3357		0.4636		0.5751

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