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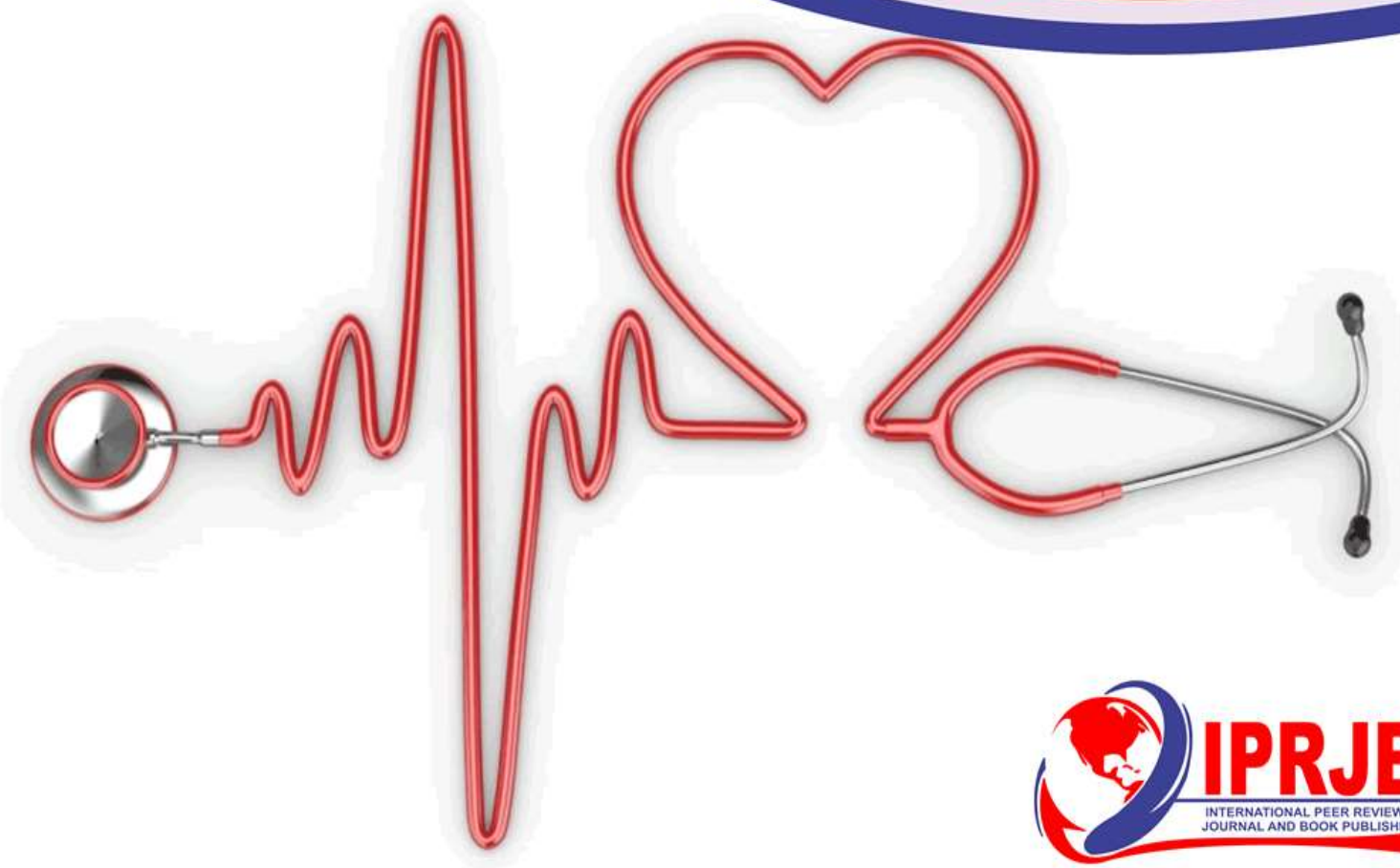

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FACTORS ASSOCIATED WITH TREATMENT SUCCESS AMONG HUMAN IMMUNODEFICIENCY VIRUS INFECTED ADOLESCENTS AT THE COASTAL GENERAL HOSPITAL, MOMBASA COUNTY

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Abstract

Purpose: Into the third decade of the HIV/AIDS epidemic, there are 34 million people living with HIV in the world, of whom five million are adolescents. AIDS is now the leading cause of death among young people in Africa and the second leading cause of death among young people worldwide. To determine factors associated with treatment success among HIV infected adolescents in the Coastal General Hospital.

Methods: This study was conducted at Coast General Hospital located in Mvita sub-County, Mombasa. An am bidirectional cohort study design was adopted. The study used 165 adolescents between 10-19 years on ARVs who were selected using systematic random sampling. Data was collected using questionnaires, interview schedule, previous records and laboratory investigations. Data analysis was done using SPSS version 20. A comprehensive summary of the associated factors to development of treatment success among HIV adolescents on ARVs was presented.

Results: The study findings established that on Morisky 4 Scale, adherence level up to 7 out 10 adolescents can be characterized as good while 3 out of 10 have adherence levels characterized as inadequate or poor. On a Morisky 8 Scale, adherence levels of up to 6 out of 10 adolescents is characterized as good while the inadequate and poor adherence levels could be as high as 9 in every 10 adolescents. Up to 7 in every 10 adolescents experience treatment success while up to around 4 in every 10 adolescents experience treatment failure. Determinants of poor adherence levels and treatment failure include having lived with HIV for a period more than a year , adherence pattern immediately after HIV status awareness, ARV uptake of more than 5 years and between 3 and 4 years respectively as well as adherence level on Morisky 4 scale.

Unique contribution to theory, practice and policy: The primary target and focus towards curbing non adherence among adolescent should be patients who have lived with HIV and been taking ARVs for more than 1 year. Interventions to enhance treatment success should focus on female gender adolescents, those who have lived with HIV for a period greater than 1 year, those who have been taking ARVs for more than 5 years and those with poor adherence level on Morisky 4 Scale.

Keywords: *Human immunodeficiency virus, highly active antiretroviral therapy, adherence, treatment success.*

1.0 INTRODUCTION

Kenya is among the top five sub-Saharan Africa countries with the highest burden of HIV a new report by University of Washington in USA has shown. The report, *The Burden of HIV: Insights from the GBD 2010*, shows the epidemic accounts for 15.3% of the national disease burden and that 18.1% of deaths in Kenya are caused by Aids-related complications. According to last the *Economic Survey*, 12,176 Kenyans died of AIDS in 2015 (Porco. *et al*., 2016). Approximately 29% of all new HIV infections are among adolescents (Kenya HIV Estimates; UNAIDS/NASCOP) AIDS is the leading cause of death and morbidity among adolescents and young people in Kenya.

HIV remains among the greatest public health concerns and the leading cause of death in Mombasa County, the epidemic has continued to cause deaths and suffering among residents, tearing the social and community fabric and decimating the workforce. The County has reduced the HIV prevalence from 11.1% (KAIS 2012) to the current estimated 7.4% in 2014. This has been through scaling up of HIV prevention education, provision of HIV testing services and also ensured treatment coverage of over 60% for those in need of ARVs in accordance with the new treatment guidelines by the World Health Organization (WHO).

Lall (2015) summarizes the factors contributing to the higher mortality among HIV-positive adolescents: the lack of awareness of sero-status, poor linkages between testing and treatment services, difficulty in retention in care and lack of adherence to antiretroviral therapy (ART) regimes. Those who acquired HIV infection perinataly have many questions unanswered and have significant psychological trauma. This age group is key, but often overlooked in managing the HIV epidemic (Meynard*et al*., 2016)

These factors may complicate adolescents' transition towards taking responsibility for managing their illness, ART adherence and clinic appointment attendance. Adolescents have been found to have poor adherence to antiretroviral therapy, with one study showing a decrease in adherence as children moved into adolescence. In addition, low levels of virological suppression, increased risk of virological failure, loss to follow-up and death have all been described (McNabb *et al*., 2011).

The Morisky Medication Adherence Scale is a validated assessment tool used to measure non-adherence in a variety of patient populations. The tool uses a series of short behavioral questions geared in such a way to avoid “yes-saying” bias commonly seen with chronic care patients. Since 2008 when research established the predictive validity of the tool in patients with hypertension. The study found a significant association between blood pressure control and the medication adherence score.2 However; this was not the first time that the Morisky Medication Adherence Scale was validated in patients with hypertension. Researchers had been developing and testing the non-adherence questionnaire for years prior to its widespread use. The tool has shown benefits of using both the MMAS-4 and MMAS-8 for different applications depending on the condition being evaluated (Morisky *et al.*, 2008).

Statement of the Problem

HIV/AIDS is the one of serious health problems and a leading cause of mortality and morbidity among HIV infected adolescents and remains among the greatest public health concerns in Mombasa County, tearing the social and community fabric and decimating the workforce. The current active clients on care in CGH is 4113.There are 34 million people living with HIV in the world, of whom five million are adolescents where 42% of all new

infections are among adolescents. An estimated 2,500 adolescents become infected with HIV/AIDS every day (Walsh *et al*., 2014).

In this group treatment success and its associated factors are often a neglected and under-recognized issue within the realm of HIV treatment, possibly because adolescents face such unique circumstances when compared to their pediatric and adult counterparts. This lack of recognition poses a severe threat given that 2.1 million adolescents are HIV-positive worldwide.

While worldwide the number of new HIV infections decreased by 44% between 2001 and 2012, there was no substantial decrease among adolescents. Furthermore, while, between 2005 and 2012, the global number of HIV-related deaths fell by 30%, it increased by 50% among adolescents. Non adherence to medication is the key obstacle to HIV treatment success. The group at highest risk of non-adherence is adolescents (Coetzee *et al*., 2012)

Although large studies of efficacy of ART in HIV-infected adults and children have been conducted, relatively few data have been collected describing factors associated with treatment success among adolescents. Low medication adherence in adolescents, the very population most likely to benefit from optimal adherence (i.e., those who would have the longest life expectancy on successful ART), underscores the urgent need to identify factors that contribute to treatment success in HIV-infected adolescents.

Such knowledge would help guide the design of targeted interventions to achieve or maintain treatment success in this population. Given the limited availability of second-line and salvage antiretroviral therapy regimens in this region, preserving long-term success of first-line ART is critical, particularly in adolescents, who would be expected to live longer than HIV-infected adults by virtue of their younger age, if both groups are able to achieve equivalent treatment success.

2.0 LITERATURE REVIEW

2.1 Level of Treatment success

Emerging drug resistance and subsequent treatment failure poses a major concern for HIV programs in resource-limited settings where treatment options are limited. Of the populations living with HIV adolescents and youths are the most dynamic and challenging group, where some infections are behaviorally acquired from experimenting with drugs and sex which is phenomenal with this age group (Bangsberg*et al*, 2005). As infected children transition to adolescence the gains of ART may be compromised because of decreased adherence to medication associated, generally with long term treatment and transition (Amos*et al*., 2005).

Previous studies in resource-limited areas have identified factors associated with decreased adherence to ART, the development of ART-resistant infection, and survival following ART. In Botswana, a study identified the cost of ART as a barrier to therapy adherence in 47 (44%) of 108 subjects, followed by other factors, including social stigma, migration and travel, and adverse effects (Harrigan*et al*., 2013). A Ugandan study found that low monthly income and married individuals were associated with decreased adherence (Ramadhani et. al, 2007).

Adolescent patients with chronic diseases generally have decreased adherence with associated increased morbidity and mortality (Foster *et al*., 2009). In a Southern Africa cohort, ART adherence was estimated to be lower in adolescents than in adults. Furthermore

adherence reduced successively with each of four estimation time points over two years follow up (Nachenga*et al.*, 2009)

In this same cohort, (Nachenga*et al.*, 2009) reported that only 28.3% of adolescents reported taking all of their prescribed antiretroviral medications in the previous month, and factor analysis revealed barriers to adherence to be medication-related adverse effects (both physical and psychological) and complications in day-to-day routines. In another U.S. study, the Pediatric AIDS Clinical Trial Group (PACTG) 381, the cohort included 120 adolescents (ages 11–22 years) infected via high-risk behaviors and treated with at least two NRTIs plus either a protease inhibitor or an efavirenz-containing HAART regimen. Of these 120 subjects, 44 (37%) stayed on study treatment for the 3 years of observation. Twenty-nine (24%) subjects reached and maintained undetectable viral loads. Poorer adherence was the main predictor of virologic failure (Hazra*et al.*, 2010).

A systematic review of the epidemiology of ART failure on a global scale by Gercia*et al.*, 2012 prevalence surveys showed inter-region and intra-region variability in part because of methodological differences. Despite this variability, a collaborative study and meta-analysis of global trends of ART treatment failure found a significant increase in prevalence of treatment failure among adolescents over time since ART rollout especially in regions of sub-Saharan Africa (Garcia *et al*., 2012).

The scale-up of antiretroviral therapy (ART) in Kenya is being undermined by high rates of treatment failure (Garcia *et al*., 2012). Over a third of patients failed first- and second-line therapy. Use of inappropriate regimens and lack of adherence support were associated with failure to control viral load (Kuritzkes*et al*.,2011).

2.2 Adherence to ART

Adherence is defined as ability of a patient to adopt behavior and attitude that serve toempower him/ her to improve health and self-manage a given illness or, ability of apatient to take all medications as prescribed with no missed dose; the right drugs, rightdosage, right time, and right way (Howard *et al*., 2012). Establishing and maintaining adherence tomedication is a difficult goal for an individual with chronic illness even when treatment regimen is simple and the patient is clearly symptomatic. Even brief episode of missed medication dose can permanently undermine HIV treatment leading to reduced efficacy and increase resistance to medication.

To reduce pill burden, adverse drug reactions, drug interaction and improve adherence, a revised new guideline on use of ARVs for treating and preventing HIV in Kenya released in 2016 recommends Tenofovir + Lamivudine + Dolutegravir/Efavirenzfor patients above 15 years as the first line regimen. The Morisky Medication Adherence Scale is a validated assessment tool used to measure non-adherence in a variety of patient populations. The tool uses a series of short behavioral questions geared in such a way to avoid “yes-saying” bias commonly seen with chronic care patients. Since 2008 when research established the predictive validity of the tool in patients with hypertension, the study found a significant association between blood pressure control and the medication adherence score. However, this was not the first time that the Morisky Medication Adherence Scale was validated in patients with hypertension. Researchers had been developing and testing the non-adherence questionnaire for years prior to its widespread use. The tool has shown benefits of using both

the MMAS-4 and MMAS-8 for different applications depending on the condition being evaluated (Morisky*et al.,* 2008).

A patient is said to have inadequate or poor adherence when:

- Morisky Medication Adherence Scale 4 (a tool to assess adherence using a standardized questionnaire for every patient in every visit) score 1-2 means inadequate adherence and 3-4 means poor adherence. Refer to appendix XIII.
- Morisky Medication Adherence Scale 8 (assess adherence using standardized questionnaire for patient with suspected adherence problems) score 1-2 means inadequate adherence and 3-8 is poor adherence. Refer to appendix XIV.
- Pill counts: Ask the patient to bring all their pills with them to follow-up visits. Calculate how many pills should be remaining based on the previous prescription date and amount prescribed ,and compare to how many pills are actually remaining .Excess pills are assumed to be missed doses. Refer to appendix XV
- Return dates: Compare drug pick-up date with expected date of pick-up (based on number of pills dispensed at last visit). If drugpick-up date is later than expected, it is assumed the patient is missing doses equivalent to the number of days late.

Non-adherence to medication is the key obstacle to HIV treatment success (Stephen *et al*., 2010). The group at highest risk of non-adherence is adolescents. In particular, those who acquired HIV infection perinataly have many questions unanswered and have significant psychological trauma. Adolescence is a key, but often overlooked, phase in managing the HIV epidemic.

Adherence data on Kenya adolescents and youth is limited but there is good indication that non adherence is high. A large study of 312335 youth utilizing routinely collected patient level data from 160 HIV clinics in Kenya recorded a substantially high attrition before and after ART initiation among youth (15-24 years) compared to other age groups (Bersenberg*et al*., 2014).

In other studies showed that up to 30% non-adherence has been estimated among HIV infected youth attending Kangemi and Coptic health clinics in Nairobi (Gitu*et al*., 2012). Along the Kenyan coast less than 95% adherence among young adults reporting high risk sexual behavior was reported from 40% of men having sex with men (MSM), 28.6% of heterosexual men, and 11.5% of females (Harrigan*et al*., 2013)

In an ideal situation, a 100% level of adherence is required for ARV treatment success (Hirsch *et al*., 2010). Though adherence is a problem in poor countries due to multifaceted factors, studies show that there is no significant difference in adherence between resource-limited and resource-rich countries, suggesting that patients have trouble in taking 100% of their pills. It is therefore recommended worldwide that for any ARV program there should be a concurrent plan for adherence assessment and support. A 'near perfect adherence' should be where there is 95% and above adherence. (Bangsberg*et al*. 2014).

Non-adherence to therapy is a major cause of drug resistance leading to treatment failure. As proposed by Friedland and Williams 2013, the relationship is thought to be "bell shaped," such that complete adherence and total non-adherence to HAART are associated with low probabilities of resistance, whereas intermediate levels of adherence increase the risk of resistance. Although the level of adherence associated with the highest risk of resistance is

unknown, it has been suggested that only marginally suboptimal adherence can lead to resistance (Friedland&William2013).

2.3 Adolescents level factors associated with Treatment success

Adolescence is a complex development phase of marked psychosocial, behavioral, physiological and cognitive changes that exacerbate the challenges of an HIV-positive status and the requirement to adhere to a structured treatment regimen (Wast*iet al*., 2012). It is a time when there is hyperawareness of physical appearance and also a time of experimentation, risk-taking and significant peer influence with a need to assert an individual identity that is distinct from caregivers. A meta-analysis of studies conducted in developing countries reported additional barriers to ART, including fear of disclosure of HIV infection status, concomitant substance abuse, forgetfulness, suspicion of treatment, complicated drug regimens, the large number of pills required, decreased quality of life, work and family responsibilities, falling asleep, and lack of access to medication (Ramadhani*et al*., 2007).

These factors may complicate adolescents' transition toward taking responsibility for managing their illness, ART adherence and clinic appointment attendance. Adolescents have been found to have poor adherence to antiretroviral therapy, with one study showing a decrease in adherence as children moved into adolescence (Mavhu*et al*., 2013).

2.3.1 Stigma and Disclosure

Stigma, both perceived and experienced, hampers adolescents from both obtaining and taking their drugs. Adolescents describe how they would avoid going to the clinic to obtain their drugs because they did not want community members to see them. At times, family members who were asked to pick up the medication refused, for fear of being seen and labeled as living with HIV (Mutwa et *al*., 2013). Furthermore they must also deal with issues such as disclosure, and practicing safe sex while also addressing issues traditionally associated with adolescence such as body image, first sexual experience, peer pressure and forming personal identity. Poor adherence is attributed to this unique physical and psychosocial evolution (Mahve*et al*., 2013).

Unlike most adult populations, adolescents face not only issues of disclosing to others, but also coming to terms when they are informed of their own HIV status. In some instances, the adolescent's HIV status is kept hidden even after s/he began ART and s/he does not exactly know what the medication is for. When the doctor or caregiver disclosed their status, it often helped the participants to realize the importance of adherence.

2.3.2 Drug and Substance abuse

Substance abuse has been widely reported to negatively affect use of antiretroviral medications. In treating HIV-1-infected substance abusers, it is commonly advocated that attempts to address substance abuse should precede initiation of potent antiretroviral therapy to maximize clinical response. Active drug or alcohol use probably impedes HIV-1 treatment in several ways. First, substance abuse is associated with lifestyle instability that is poorly conducive to stringent adherence to therapy. Second, substance abuse is associated with poor social support, mistrust of the medical establishment, non-adherence with scheduled clinic visits, and overuse of emergency care services. Third, medical providers are frequently uncomfortable caring for substance abusers. Last, substance abuse is associated with depression and other mental health disorders, which have been commonly cited as barriers to

adherence. Screening for and treating mental health disorders remains an important intervention in all HIV-1-infected adolescents (Lucas et *al.*, 2012).

The first large-scale disease progression study in the U.S. of HIV-positive adolescents infected through sexual behavior or injection drug use, called REACH (Reaching for Excellence in Adolescent Care and Health), found that only 41% of adolescents (ages 12–19 years) on ART reported >95% adherence and that factors associated with poor adherence included depression, pill burden, advanced HIV status, alcohol use, and dropping out of school.

2.3.3 Social-support and Structures

Besides adolescence being a turbulent and vulnerable period in life with many physical and emotional changes, factors, such as being orphaned or school conditions may pose extra challenges. Several adolescents experience difficulties in having one HIV-infected child and the others healthy, thus becoming a challenge to remain adherent when most of the siblings are unaware of the HIV status. However, living situations may cause the most issue for ART adherence for these adolescents. When adolescents are living with their own family, they feel their family members, including parents and siblings, generally provide a supportive environment, often reminding them to collect and take their medication, however orphan adolescents living in foster families may not have the same level of support from their foster parents as they would from their own parents and that stigma in their own home may lead them to take their medication less (Mutwa et *al*., 2013).

Religious support and practices, such as fasting, religious healing or cure may influence ART adherence. Adolescents living with HIV who live in boarding schools ART adherence is a complex situation. Schools may not accommodate their ART needs, making it difficult for them to access their medication. Further, students sometimes have conflicts with their medication schedule and their class schedule thus leading to students becoming non-adherent (Pool et *al*., 2013). In addition to this, physical or sexual violence is on the increase in Kenya with 50% of the women aged 15-49 years have experience violence in their lifetime.(Kenya National Bureau of Statistics and ICF 2014). In Kenya a recent study showed 32%0f young women aged 18-24 years and 18% of their male counterparts reported experiencing sexual violence before age of 18 (Bangsberget et *al.*,2015). GBV reduces the bargaining power to negotiate safer sex, stay on treatment or remain in school.

2.4 Conceptual framework

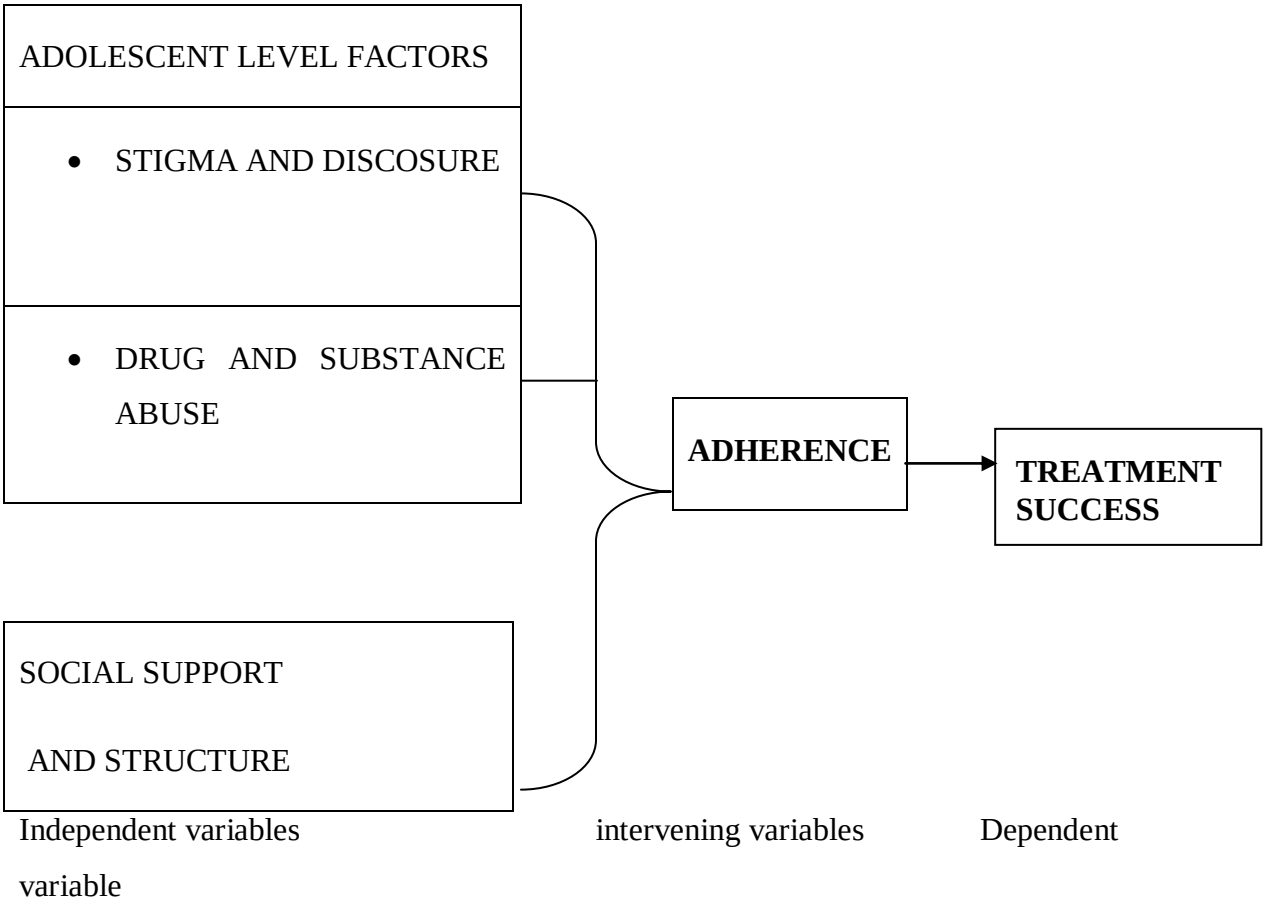

Figure 1: Shows relationship between dependent and independent variables

3.0 MATERIALS AND METHODS

The study was implemented in Mombasa County. The county has a total population of 1.3 million according to Kenya Bureau of Statistics National Census report 2019. The HIV prevalence is 11.1% with a total of 66542 adults and 10630 children living with HIV in the County. The study was conducted in the Coastal General Hospital Compressive Care Clinic. This study used an ambidirectional cohort study design by using both retrospective and prospective data collection methods. The study population was HIV infected adolescents between 10-19 years old accessing HIV services at the Coastal General Hospital who were initiated HAART for at least six months and who were on first line ART regimen only. The study used 165 adolescents between 10-19 years on ARVs who were selected using systematic random sampling. The sample size was determined according to Cochran, W. G. (1977). The 10-19 year age group is of interest because 29% of new infections occur in this group compounded by documented challenges. (Foster et. al., 2014). Participants were recruited from the CCC register in Coast General Hospital who were on first line ART regimen and included adolescents between 10-19 years who consented to the study. To ascertain eligibility their age and ART status were confirmed from the patient files. For those with persistently high viral load ≥ 1000 copies/mL (two viral loads measured within a 3

month interval with adherence support between measurements) after at least 6 months of using ART were termed as failing treatment. The main tool for determining treatment success in this study was lab investigation, the viral load test. This was preferred to the CD4 cell test because it's reliable, accurate and more specific. Progressively falling CD4 and development of OIs gave a high index of suspicion therefore a viral load test was highly recommended for confirmatory treatment failure or success.

Data was collected using questionnaires, interview schedules, from CCC registers and laboratory investigations. The degree of adherence by individual patients was estimated through pill counts, pharmacy refill records included counter checking the expected return date from the patient's card. Morisky adherence form 4 and 8 was used to assess level adherence. Laboratory investigation was performed for the subjects with no viral load results, after 3 months for patients with viral load of above ≥1000 cop/ml or if the available results are more than six months old. Data was checked daily for completeness, then edited, coded and entered in Microsoft Excel before exported to SPSS for analysis. Quantitative data was analyzed using SPSS version 20. Univariate analysis was performed using logistic regression to identify factors associated with treatment success. The criteria for selection of variables possible for inclusion in multivariable analysis were based on p-value of less than 5%. The strength of association was measured using Odds Ratios (OR).

4.0 RESULTS

All the 165 respondents who were targeted for this study were successfully interviewed; hence 100% response rate was achieved.

Table 1: Demographic Information for the study population

		n (%)
Gender	Male	45 (27)
	Female	120 (73)
Sub Total		165(100)
Age	10-13	30 (18)
	14-17	52(32)
	>17 yrs	83 (50)
Sub Total		165 (100)
Education	None	16 (10)
	Primary	61 (37)
	Secondary	68 (41)
	Tertiary	20 (12)
Sub Total		165 (100)

4.2 Viral Load results for the study participants

At baseline, 112 (68%) of the subjects had viral load of ≤ 1000 whereas 53 (32%) recorded above 1000 viral load count. At follow up, 42 (79%) had viral load of ≤ 1000 whereas 21 (11%) recorded above 1000 viral load count.

Table 2: Viral Load results for the study participants

		Initial n (%)	Final n (%)
Viral Load	≤1000	112 (68)	42 (79)
	>1000	53 (32)	11 (21)
TOTAL		165 (100)	53(100)

4.3 Tests of Association

Univariate analysis was performed using logistic regression to identify factors associated with treatment success. The criteria for selection of variables possible for inclusion in multivariable analysis were based on p-value of less than 5%. The strength of association was measured using Odds Ratios (OR).From the results as shown in table 3, the period lived with HIV, duration of ARV uptake, adherence after HIV status awareness have significant association with ARV medication adherence and treatment success.

4.3.1 Determinants of Adherence to ART among the study participants– univariate analysis

Those who have lived with HIV for less than 1 year have higher chances of good adherence to ART compared to those who have lived with HIV for a year or more. Those who have lived with HIV for a period between 1 and 5 years are 91% (OR 0.09) less likely to adhere well compared to those who have lived with HIV for less than a year (p-value 0.023). Having lived with HIV for a period of 6-10 years reduces the probability of good adherence by 33% (OR 0.67) compared to patients who have lived with HIV for less than a year (p-value 0.014). Further, having lived with HIV for a period of 11-15 years reduces the probability of good adherence by 14% (OR 0.86) compared to patients who have lived with HIV for less than a year (p-value 0.033). Finally, patients who have lived with HIV for more than 15 years are 90% (OR 0.10) less likely to adhere well to ART compared to those who have lived with HIV for less than a year (p-value 0.059).

Duration of ARV drugs uptake also has a significant association with adherence level of HIV patients. Specifically, those who have taken ARV medication for more than 5 years are 97% (OR 0.03) less likely to adhere well compared to those who have taken ARV medication for less than 1 year (p-value 0.053). Although not statistically significant, taking ARV drugs for a period between 1 and 5 years equally reduces good adherence likelihood by up to 60% (OR 0.4) with the least expected reduction in likelihood being 30% (OR 0.7); these compared to those who taken ARV medication for less than 1 year.

Upon becoming aware of their HIV status, some patients admitted that they strictly adhered well while others stopped taking their ARVs. This was established to have a significant association with future adherence levels as those who stopped taking medication are 90% (OR 0.1) less likely to continue with good adherence compared to those who adhered well upon becoming aware of their HIV status (p-value 0.000).

Table 3: Determinants of Adherence to ART among the study participants

		N		OR (95% CI)	P-Value
		Poor	Good		
Period Lived with HIV	< 1 yr.	1	15	1	
	1-5 yrs	41	56	0.09 (0.1-0.7)	0.023
	6-10 yrs	13	13	0.67 (0.01-0.6)	0.014
	11-15 yrs	7	9	0.86 (0.01-0.8)	0.033
	> 15 yrs	4	6	0.1 (0.01-1.1)	0.059
Duration of ARV Uptake	< 1yr	6	17	1	
	1-2	22	27	0.4 (0.2-1.3)	0.132
	2-3	9	18	0.7 (0.2-2.4)	0.578
	3-4	9	18	0.7 (0.2-2.4)	0.578
	4-5	6	7	0.4 (0.1-1.7)	0.225
	>5 yrs	14	12	0.3 (0.1-1.0)	0.053
Adherence After Awareness	Adhered Well	30	90	1	
	Stopped Taking	36	8	0.1 (0.03-0.2)	0.000

4.3.2 Distribution of level of adherence to ART among the study participants – Multivariate Analysis

While controlling for the variables that had significant influence on ART adherence, the period lived with HIV, duration of ARV uptake as well as strict adherence upon status awareness were identified as risk factors for non-adherence. While controlling duration of ARV uptake as well as status of adherence upon awareness to HIV status, the period lived with HIV significantly influences adherence patterns for patients who have lived with HIV for a period between 1 and 10 years compared to those who have lived with HIV for less than 1 year. Patients who have lived with HIV for a period between 1 and 5 years are 99.2% (OR 0.008) less likely to adhere well compared to those who have lived with HIV for less than 1 year (P-value .002). Likewise, while controlling for duration of ARV uptake as well as status of adherence upon awareness of one's HIV status, patients who have lived with HIV for a period between 6 and 10 years are 99.0% (0.010) less likely to adhere well compared to those who have lived with HIV for less than 1 year (P-value .007).

Also, while controlling the period lived with HIV and duration of ARV uptake, adherence status upon becoming aware of HIV status increases reduces the chances of adherence by 97.3% (OR 0.027, P-value .000). The duration of ARV uptake has no statistical significance on adherence status while controlling for the period lived with HIV and adherence upon status awareness.

Table 4: Distribution of level of adherence to ART among the study participants – Multivariate Analysis

		P-Value	OR	95% C.I. for OR Lower	Upper
Period Lived with HIV	< 1 Yr		1		
	1-5 yrs	.002	.008	.000	.174
	5-10 yrs	.007	.010	.000	.281
	10-15 yrs	.066	.031	.001	1.263
	>15 yrs	.127	.045	.001	2.416
Duration of ARV Uptake	< 1 yr		1		
	1-2 yrs	.145	3.840	.628	23.496
	2-3 yrs	.059	6.544	.934	45.825
	3-4 yrs	.081	5.945	.803	43.993
	4-5 yrs	.144	7.578	.501	114.674
	> 5 yrs	.165	7.895	.428	145.552
Adherence After Awareness	Adhered Well		1	-	-
	Stopped Taking	.000	.027	.007	.111

4.4 Treatment Success – Univariate Analysis

4.4.1 Distribution of factors associated with Treatment Success among the study participants– Univariate Analysis

From the results as shown below, the period lived with HIV, duration of ARV uptake, adherence after HIV status awareness, having had other opportunistic disease and adherence level are significant determinants of treatment outcome.

Those who have lived with HIV for more than 1 year have higher chances of treatment failure or less likelihood of treatment success compared to those who have lived with HIV for less than a year. Having HIV for a period between 6 and 10 years statistically reduces the chances of treatment success by 93% (OR 0.07) compared to those who have lived with the disease for less than a year (p-value 0.014). Although not significant enough, those who have lived with HIV for a period between 1 and 5 years have the chances of treatment success reduced by 85% (OR 0.15) compared to those who have lived with the disease for less than a year (p-value 0.071). Likewise, living with HIV for a period between 11 and 15 years reduces likelihood treatment success by 89% (OR 0.11) compared to living with HIV for less than a year (p-value 0.057). Also, despite being statistically insignificant, living with HIV for more than 15 years also reduces the chances of treatment success by 84% (OR 0.16) compared to living with HIV for less than a year (p-value 0.134).

It is also noted that having taken ARV therapy medication for a period between 3 to 4 years (p-value 0.033) as well as more than 5 years (0.045) both statistically reduces treatment success by 97% (OR 0.3) compared to being under medication for a period less than a year. Also, although statistically insignificant, those who have been under medication for a period between 4 and 5 years have a 50% (OR 1.5) increased chances of treatment success compared to those who have taken ARVs for less than a year. However, patients who have taken ARVs for a period between 2 and 3 years have 3% (OR 0.97) reduced chances of treatment success compared to those who have been under medication for a period less than a year.

Patients who began strict adherence immediately upon becoming aware of their HIV status have higher chances of treatment success compared to those who stopped taking ARV

medication (p-value 0.000). Stopping ARV medication reduces treatment success by 97% (OR 0.3) compared to strictly adhering to treatment upon HIV diagnosis.

Having other opportunistic diseases including TB, Pneumonia, H. Zooster and/ or Meningitis increases the chances of treatment failure or reduces the chances of treatment success by 96% (OR 0.4) compared to when there's no opportunistic disease (s) (p-value 0.021).

Good adherence levelon Morisky 4 scale increases the likelihood of treatment success 7 times (OR 7.6) compared to having poor (moderate or poor) adherence levels on Morisky 4 scale (p-value 0.000).

Table 5: Determinants of Treatment Success among the study participants– Univariate Analysis

		N		OR (95% CI)	P-Value
		Failure	Success		
Period Lived with HIV	< 1 yr.	1	15	1	
	1-5 yrs	30	67	0.15 (0.02-1.18)	0.071
	6-10 yrs	13	13	0.07 (0.01-0.58)	0.014
	11-15 yrs	6	10	0.11 (0.12-1.07)	0.057
	> 15 yrs	3	7	0.16 (0.01-1.78)	0.134
Duration of ARV Uptake	< 1yr	5	18	1	
	1-2	13	36	0.8 (0.2-2.5)	0.662
	2-3	6	21	0.97 (0.3-3.7)	0.967
	3-4	14	13	0.3 (0.1-0.9)	0.033
	4-5	2	11	1.5 (0.3-9.3)	0.645
	>5 yrs	13	13	0.3 (0.1-0.97)	0.045
Adherence After Awareness	Adhered Well	29	91	1	
	Stopped Taking	24	20	0.3 (0.1-0.6)	0.000
Other Disease Suffered	No	36	94	1	
	Yes	17	18	0.4 (0.2-0.9)	0.021
Adherence Level (Morisky 4)	Good	53	0	1	
	Poor	0	112	7.6 (3.7-15.9)	0.000

4.4.2 Distribution of factors associated with Treatment success among the study participants – Multivariate Analysis

While controlling for the variables that significantly determine treatment success, adherence level on Morisky 4 scale remains the only significant determinants of treatment success with an increased 7 fold chances of treatment success among patients with good adherence compared to those who have poor (moderate or poor) adherence levels (OR 7.009, P-value .000).

Table 6: Determinants of Treatment success among the study participants – Multivariate Analysis

		P-Value	OR	95% C.I. for OR	
				Lower	Upper
Period Lived with HIV	< 1 yr.		1		
	1-5 yrs	.154	.136	.009	2.114
	6-10 yrs	.090	.070	.003	1.507
	11-15 yrs	.287	.161	.006	4.662
	> 15 yrs	.527	.303	.008	12.194
Duration of ARV Uptake	< 1yr		1		
	1-2	.155	3.803	.604	23.953
	2-3	.178	3.935	.535	28.932
	3-4	.768	.741	.101	5.427
	4-5	.058	12.928	.913	183.103
	>5 yrs	.784	1.453	.100	21.082
Adherence After Awareness	Adhered Well		1		
	Stopped Taking	.462	.662	.221	1.984
Other Disease Suffered	No		1		
	Yes	.073	.415	.158	1.087
Adherence Level	Good		1		
	Poor	.000	7.009	2.644	18.582

5.0 DISCUSSIONS, CONCLUSIONS AND RECOMMENDATIONS

Discussions

Among the subjects, around one third (27%) were male while around two thirds (73%) were female. In both the univariate and multivariate analysis, gender was an insignificant determinant of both treatment adherence and success. This is consistent with a study by Ammassari*et al*., (2002) which did not find any association between adherence to ART and sex. However, a study by Mellins*et al.* (2004) established male gender as important factors which affect adherence. Although not statistically significant, this study established that the chances of good adherence increases with being a female by 1.1 folds compared to being a male. This contrasts with Mellins*et al.* (2004) findings that associated the odds with the male. On the contrary, this study also established that being a female reduces treatment success by 0.6 folds compared to being a male.

The study also established that 18% of the subjects were aged between 15 and 18 years, 32% were aged between 19 and 21 years whereas 50% i.e. half of the participants were aged between 22 and 24 years. Influence of age on adherence and treatment success was found to be insignificant. Despite this, good adherence and treatment success favored old age (22-24 years) with those in this age group being 1.2 times more likely to adhere well than those aged below 18 years and 1.3 times more likely to experience treatment success than below 18 years counterparts. Some studies have however associated age with adherence. For instance, Sharada*et al.* (2012) associated good adherence with age below 35 years whereas Orrell *et al.* (2003) associated non- adherence with adolescent age. It therefore means age may or may not be a determinant factor depending on the contexts and other competing factors that may act as confounders.

Education level was found to be an insignificant factor on both adherence and treatment success. However, the odds of adherence among those holding Tertiary education levels were 1.1 times higher than those with no education background. Also, compared to those with no

education background, the chances of treatment success were higher among those with Primary school education (OR 1.4) followed by Secondary (OR 1.3) then Tertiary (OR 1.1). Previous studies have however associated education level with adherence levels with the odds of non-adherence increasing with low education level. Bonolo *et al.,* (2005) while studying non-adherence among patients initiating antiretroviral therapy: a challenge for health professionals in Brazil noted that being illiterate is associated with increased likelihood of non-adherence to ART. Despite education being an insignificant determinant of adherence as found in this study, the findings on the association between higher education level and good adherence remain consistent with previous studies. Johnson*et al.,* (2010) attributes this to the fact that patients with limited literacy might be reluctant to ask others for the kind of help they need to take their medicines correctly. Sharada*et al.,* (2012) also argued that education may impact on adherence in several ways including facilitating communication with health care providers, increasing retention of information provided by health workers and thereby enhancing adherence to ART medication.

On marital status, the married and singles included 28% and 42% among the participants. Likewise, those divorced and cohabiting included 6% and 24%. The married were considered as 'Partnered' in the logistic regression test while others were considered as those with 'No Partner'. Marital status was an insignificant factor on both adherence and treatment success although it was noted that those without partners were more likely to adhere well than those with partners (OR 0.8) while treatment success is favored those with partners (OR 1.5). These findings are in congruent with the study findings by Boniphace *et al.* (2012) who found no association between marital status and adherence but noted that the single, divorced, widow or separated are 1.5 times likely to be non-adherent to treatment regimen compared to the married/ cohabiting. It's been known that having a partner plays a role in supporting and reminding the patient to take drugs. In fact, the study noted that patients who had not lost any parents were twice likely to adhere well than those who had lost their mothers (OR 0.5) or both parents (OR 0.5). Further, this study established that losing a mother (OR 0.5), father (OR 0.95) or both parents (OR 0.85) reduces chances of treatment success compared to when a patient has both parents alive. It has been shown that good social support helps HIV-positive patients handle stigma and discrimination better (Liamputtong, *et al.* 2009).

On occupation, employed and the unemployed were found to be 1.7 and 1.5 times more likely to adhere to medication than those in Business. The employed had the worst adherence levels (OR 0.6) compared to those in Business as well as other occupations. Occupation was however an insignificant factor on adherence and treatment success. Despite finding employment status as an insignificant factor, Boniphace *et al.* (2012) noted that being unemployed slightly increases the odds of non-adherence by 1.1 folds. However, Sharada*et al.,* (2012) found a significant association between employment status and adherence with the unemployed being 3.5 times more likely to adhere than the employed Patients. This can be attributed to the competing tasks and interests at work place or occupation that may results to the patients either forgetting or left with no time to take their medication.

The period lived with HIV was found to be a significant determinant of both adherence and treatment success. Having lived with HIV for a period between 1 and 5 years, 6-10 years and 11-15 years reduces the odds of good adherence by 0.09 (p-value 0.023), 0.67 (p-value 0.014), and 0.86 (p-value 0.033) folds respectively. Despite being insignificant, living with HIV for more than 15 years equally reduces the chance of good adherence by 0.1 folds (p-

value 0.059). It therefore means that good adherence is associated with having lived with HIV for a period less than a year. Likewise, the duration of taking ARVs was also found to significantly influence both adherence and treatment success; i.e. taking ARV for a duration more than 5 years increases the chances of non-adherence compared to taking ARVs for less than a year. Furthermore, taking ARVs for a period between 3-4 years and more than 5 years was associated with reduced treatment success rate compared to taking ARVs for less than a year. Further analysis using Pearson Correlation test revealed that there was a significant positive correlation between period lived with HIV and duration of taking ARVs among the patients (p-value 0.000). These findings are in parallel by the study findings by Sharada*et al.*, (2012) which established that those who had been taking ARVs for 24 months or less were 2.2 times more likely to be adherent to medication than those who had been taking for more than 24 months. It therefore means that period lived with HIV and duration of taking ARVs work together to determine the adherence pattern and treatment outcome.

The study also sought to determine adherence level of patients taking different types of medication. No significance was found between the type of medication and adherence or treatment success. However, despite the insignificance, few variances were noted in the effect of each drug on adherence as well as treatment success. Those taking ABC3TCLPVr (OR 0.5) were found to be less likely to adhere to medication compared to those taking AZT3TCNVP whereas those taking TDF3TCEFV are 1.3 times likely to adhere to medication compared to patients taking AZT3TCNVP (OR 1.3). On the contrary, those taking ABC3TCLPVr were found to be 2.5 times likely to experience treatment success compared to those taking AZT3TCNVP while patients taking TDF3TCEFV and AZT3TCEFV were found to be 1.4 and 1.3 times more likely to have treatment success compared to those taking AZT3TCNVP. A patients is most likely to experience treatment failure while taking TDF3TCNVP compared to taking AZT3TCNVP. Type of regimen has been associated with pill burden due to number of pills, drug effects and/ or medication schedules. These variations and burden-effects could be attributed to the adherence levels and consequently treatment success or failure. In fact, although not statistically significant, the study noted that taking medication twice daily reduces chances of adherence by 0.6 folds compared to taking once a day. Furthermore, taking medication twice a day reduces chances of medication success by 0.8 folds compared to taking once a day. Complicated regimen (Mukhtar-Yola*et al.*, 2006) to be followed, such as the need for daily administration, dietary restriction, drug interactions, frequency of dosing, dosage, and therefore pill burden or amount of liquid, also influence adherence to therapy (Gibb*et al.*, 2003; Byrne *et al.*, 2002; Gavin and Yogev, 2002).

Beginning medication and maintaining adherence thereafter was found to be a significant determinant of adherence and treatment success. Stopping or failing to maintain adherence reduces adherence level later by 0.1 folds while reducing treatment success by 0.3 folds. Some of the known barriers that prevents immediate start of medication include denial, stigmatization and misconception about ARVs among others. The study established that 82% of the subjects had disclosed their status while 18% had not. In addition 38% had not disclosed their statuses to anyone due to lack of readiness to do so. Furthermore17% were due to fear of stigmatization and discrimination, fear of hurting family members (38%) and/ or fear separation with spouse (7%). It is therefore evident that some patients still live in denial and fear, a factor that can potentially jeopardize start of ART, adherence and treatment outcome. Disclosure for instance was significantly related to adherence (Boniphace*et al.*

2012) and this was attributed to perceived stigma in the study population. Mills*et al.,* 2006 also noted that fear of disclosure to be among the barriers to adherence in African settings.

Despite substance use being an insignificant factor influencing treatment outcome and adherence level, use of drugs increases chances of non-adherence by 2 folds (OR 0.5) while reducing treatment success chances by 0.7 folds. Drug abuse and alcohol consumption are factors that further threaten proper adherences to ART (Ayalu and Sibhatu, 2012). Studies have consistently shown that active alcohol use and substance abuse makes it more difficult for patients to adhere to treatment (Weiser*et al.,* 2006; Chander*et al.,* 2006; Braith waite*et al.,* 2005). For instance, in Botswana nearly 40 percent of the patients surveyed admitted missing a dose because of alcohol consumption (Kip*et al.,* 2009). Similar studies also indicate that alcohol is highly related to reduce adherence (Gill *et al.,* 2005). A systematic review in 2009 found that HIV/AIDS patients who used alcohol are 50–60% more likely to adhere less to their prescribed medications (Hendershot*et al.,* 2009).

Having other opportunistic diseases including TB, Pneumonia, H. Zooster and/ or Meningitis increases the chances of treatment failure i.e. treatment success is reduced by 0.4 folds with opportunistic diseases compared to when there's no opportunistic disease (s) (p-value 0.021). The opportunistic diseases also affects adherence negatively with those unaffected being 1.8 times more likely to adhere well compared to the affected. This can be attributed to implications that presents with the opportunistic diseases including the health effects on patients and extra pill burdens involved that have been associated with non- adherence as explained above. According to Paterson *et al.,* (2000) and Zaccareli*et al.,* (2005), adherence of more than 95% is needed to achieve the desired virologic suppression and prevention of opportunistic infections.

Conclusions

From the findings of this study, the following conclusions are made: On Morisky 4 Scale, adherence level among up to 7 out 10 adolescents can be characterized as good while 3 out of 10 have adherence levels characterized as inadequate or poor. On a Morisky 8 Scale, adherence levels of up to 6 out of 10 adolescents and young adults is characterized as good while the inadequate and poor adherence levels could be as high as 9 in every 10 adolescents. Up to 7 in every 10 adolescents and young adults experience treatment success (VL ≤1000) while up to around 3 in every 10 adolescents and young adults experience treatment failure (VL >1000). Determinants of poor adherence levels include having lived with HIV for a period more than a year (i.e. between 1 and 11 years), ARV uptake of more than 5 years and adherence pattern immediately after HIV status awareness. Determinants of treatment failure include having lived with HIV for a period more than a year (i.e. between 1 and 15 years), ARV uptake for a period between 3 and 4 years as well as more than 5 years, adherence pattern immediately after HIV status awareness as well as adherence level on Morisky 4 scale.

Recommendations

From the study findings, the following interventions are recommended: The primary target and focus towards curbing non adherence among adolescents and young adults should be patients who have who have lived with HIV for more than 1 year and patients who have been taking ARVs for more than year. Other focus and targets to consider in curbing non adherence are individuals aged below 18 years, those taking ABC3TCLPVr regimen, patients

taking medication twice daily, patients who have lost a mother or both parents, patients using substance, Patients whose ART have been changed and patients who have suffered or suffering other opportunistic diseases. Interventions against treatment failure should focus on female gender adolescents, those employed, and those in business, those who have lived with HIV for a period greater than 1 year, patients who have been taking ARVs for more than 5 years, patients who have lost parents, those on TDF3TCNVP regimen, suffered other opportunistic diseases, with poor adherence level on Morisky 4 Scale.

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