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INSTITUTE OF HEALTH SCIENCES

DEPARTMENT OF NUTRITION AND DIETETICS

NUTRITIONAL ASSESSMENT of HIV POSITIVE INDIVIDUALS

MASTER THESIS

BURCU YAVUNÇ

THESIS ADVISOR

Assist. Prof. Dr. İSKENDER KARALTI

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		İMZA
Başkan	: Yrd.Doç.Dr.İskender KARALTI	
Üniversite	:Yeditepe Üniversitesi	.....
Üye	: Prof.Dr. Serdar Öztezcan	
Üniversite	: Yeditepe Üniversitesi	.....
Üye	: Yrd. Doç.Dr. Can ERGUN	
Üniversite	: Bahçeşehir Üniversitesi	.....
Üye	:	
Üniversite	:	.....
Üye	:	
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Prof. Dr. Bayram YILMAZ
Sağlık Bilimleri Enstitüsü Müdürü

ÖZET

Beslenme ve hastalıklar arasında güçlü bir ilişki bulunmaktadır. İyi beslenme, güçlü bağışıklık sisteminin altın kuralıdır. Kişinin vücudunu oluşturan elementler besinlerle alınan bileşenlerdir. Bu durumda bireyin sağlığını koruyabilmesi için yeterli ve dengeli beslenmesi gerektiğini söyleyebiliriz.

Hasta kişinin içinde bulunduğu katabolik süreç, kişinin enerji ihtiyacını dolaylı olarak da makro besin öğeleri ihtiyacını arttırır. HIV pozitif bireyin yaşadığı katabolik süreçte özellikle protein yıkımları olur. Akut dönemde ve AIDS fazında malnütrisyon görülme oranı oldukça yüksektir. Kişinin medikal tedavi yanında gerektiğinde besin desteği de alması önemlidir.

Malnütrisyon dışında proteaz inhibitörüne bağlı antiretroviral terapi (ART) ve yüksek derecede aktif antiretroviral terapinin (HAART) kullanımı HIV pozitif kişinin ömrünü uzatmakla beraber karşımıza farklı beslenme sorunları da çıkartmaktadır. Vücutta yağ dağılımının farklılaşmasıyla oluşan lipodistrofi gibi metabolik sendromlar oluşmaktadır.

Bu tez çalışmasında, çalışmaya dahil olan HIV pozitif bireylerin genel sağlık durumları, HIV pozitif olma ve tedavi süreçleri, kullanılan ilaçlar ve yaşanan yan etkiler sorgulandı. Ankette bulunan 24 saatlik besin tüketim kaydı ile kişilerin beslenme alışkanlıklarına ulaşıldı. Böylece vücut kitle indeksleri ile beslenme durumları saptandı.

Sonuç olarak; HIV pozitif bireylerin günlük alması gereken enerji miktarlarını karşılamadıklarını, buna ragmen BMI değerlerinin genelinde normal sonuçlar elde edildiğini görüldü. Sebep olarak ise düşük bazal metabolizma hızı, sedenter yaşam veya kişilerin psikolojik durumu olarak gösterilebilir. Populasyonun yarısından fazlasının (%51) besin destekleri kullandığı saptandı. Ayrıca iştah düzeylerinin düşük olduğu saptandı. Populasyonun yarısından fazlası (%55,1) herhangi bir sindirim problem olmadığını söylerken, kalan kişilerin sindirim sistemi problem olduğu görüldü.

Anahtar sözcükler: HIV, beslenme, malnütrisyon,

ABSTRACT

There is a strong relationship between nutrition and illness. Good nutrition plays a vital role for the immune system. The body's components are the elements which people consume from foods. So we can say that the person should have an adequate and balanced diet.

The patient during the illness has a catabolic process which increases the both energy and other nutrient needs. During this catabolic process, the protein destruction commonly occurs. The acute phase of HIV and the stage of AIDS, frequency of malnutrition is highly common. This is important that the nutritional support is vital for the HIV positive person while taking medical therapy.

Both ART and HAART provide longer life to the HIV positive individuals. Beside of the malnutrition, these two therapies causes some other nutritional problems. The nutritional problems can be body fat distribution disorder based such as lipodystrophy or other metabolic syndromes.

In this thesis study, general health status, being HIV positive and medical therapy process, the drugs and side effects are questioned. Also the 24 hour recall survey is applied. With this survey, the nutritional habits are determined. BMI is calculated and compared to nutritional status.

As a result; it is obtained that HIV-positive individuals don't supply the required amount of energy to take daily, across to this, the BMI results showed normal values. The causes of this situation can be the low metabolic rate, sedentary life or psychological status of the HIV positive individuals. More than half of the population (51%) were found to use nutritional supplements. Also revealed that the population has low levels of appetite. More than half the population (55,1%) say that there are no digestive problems in their digestive systems, but the other part of the population has digestive system problems.

Key words: HIV, nutrition, malnutrition,

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Burcu

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LIST of ABBREVIATIONS

AIDS Acquired Immunodeficiency Syndrome

ART Antiretroviral Treatment

BMI Body Mass Index

CDC Centers for Disease Control and Prevention

CD4 Main target cells for HIV, the number of which decreases during HIV infection

FANTA Food and Nutrition Technical Assistance

FAO Food and Agriculture Organization of the United Nations

HAART Highly Active Antiretroviral Therapy

HEBI High Energy Bar for Integrated Management of Acute Malnutrition

HIV Human Immunodeficiency Virus

IU International Units

PIs Protease Inhibitors

PLWHA People Living with HIV/AIDS

PLHIV People Living with HIV

RDA Recommended Daily Allowance

REE Resting Energy Expenditure

RMR Resting Metabolic Rate

RUTF Ready to Use Therapeutic Food

TAG WHO Technical Advisory Group on Nutrition and HIV/AIDS

TDEE Total Daily Energy Expenditure

UNAIDS The Joint United Nations Programme on HIV/AIDS

UNICEF United Nations Children's Fund

WFP World Food Programme

WHO World Health Organization

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1. INTRODUCTION

Nutrition plays a vital role in human life. Especially the absence of health, it becomes more important. Acute and chronic diseases are the causes of increased

catabolic process. This means the body's nutrient requirements increase critically.

There are complex interactions between nutrition and HIV/AIDS. HIV breaks down the immune system and it causes to malnutrition. Malnutrition worsens the effects of HIV and contributes to high progression to AIDS. HIV also has a negative impact on food and nutrition. In fact, HIV/AIDS and food consumption are closely interlinked. HIV/AIDS leads to lower food consumption because of the disease's complications such as mouth sores, nausea etc. When these complications are occurred, solutions which can prevent the decrease of the nutrient intake will be lifesaving.

In this study, general and nutritional information are collected from HIV positive individuals. With this information, nutritional status and the habits are criticized and explained statistically. HIV positive individuals have higher macronutrient and micronutrient requirement which is caused by the infection. When the increased energy need couldn't supply, weight loss and the other catabolic period starts or gets faster. The survey results help to explain why the weight loss might be occurred or how it affects the other metabolic periods in the body. With the result of 24 hour diet recall records the health care professionals have a board perspective about the patients' nutrition and the related periods of HIV/AIDS.

1.1 EPIDEMIOLOGY OF HIV

1.1.1 GLOBAL LOOK

Human immunodeficiency virus (HIV) infection is one of the major global health problems.

The World Health Organization (WHO) reported that there were approximately 35 million people worldwide living with HIV and AIDS in 2013. Of these, 3.2 million were children (<15 years old) and the 2.1 million individuals worldwide became newly infected with HIV in 2013. This includes over 240,000 children (<15 years). Most of these children live in sub-Saharan Africa and were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.

A UNAIDS report shows that 19 million of the 35 million people living with HIV today have no idea about why they have the virus. The vast majority of people living with HIV are in low- and middle-income countries. According to WHO, sub-Saharan Africa is the most affected region, with 24.7 million people living with HIV in 2013. 71% of these people are living with HIV in the world live in this region.

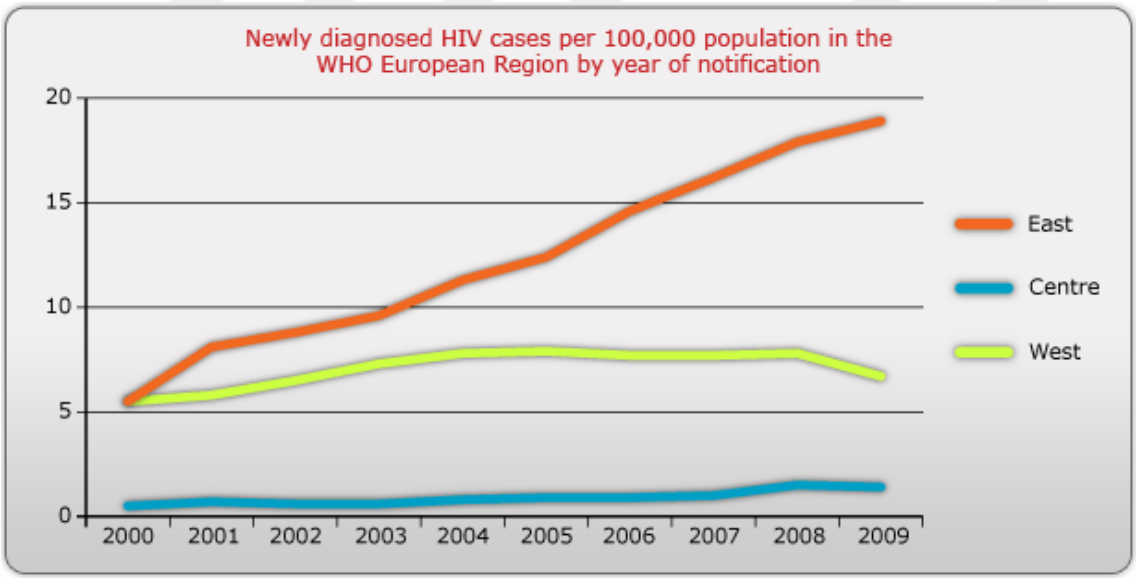

Figure 1. Newly Diagnosed HIV cases per 100.000 population in the WHO European Region by year

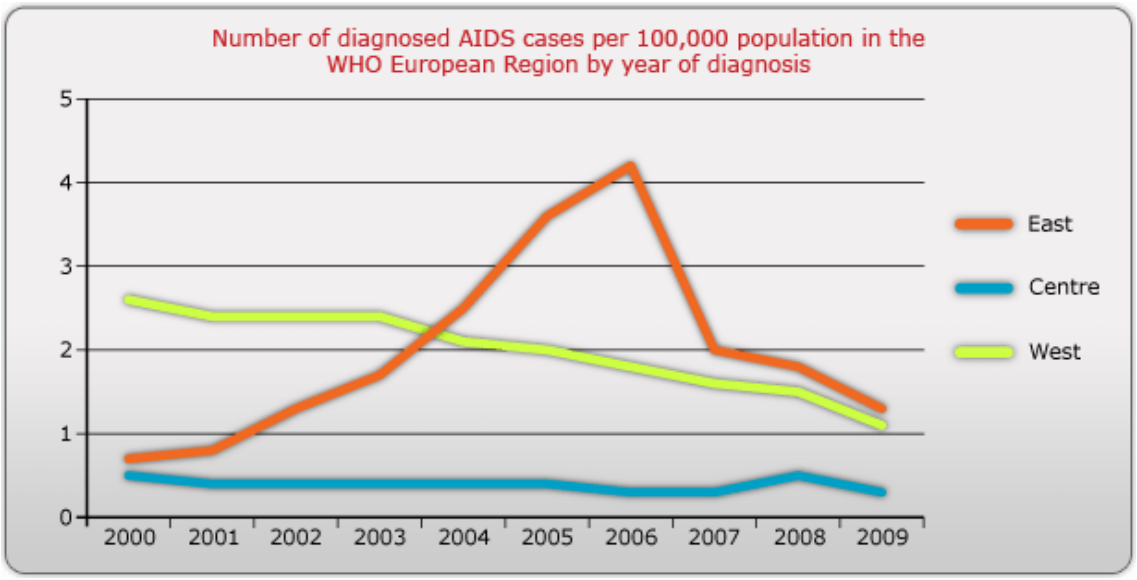

Figure 2: Number of Diagnosed AIDS cases per 100.000 population in the WHO European Region by year of diagnosis

HIV is the world's leading infectious killer. According to WHO, an estimated 39 million people have died since the first cases were reported in 1981 and 1.5 million people died of AIDS-related causes in 2013.

Even today, despite advances in our scientific understanding of HIV and its prevention and treatment as well as years of significant effort by the global health community and leading government and civil society organizations, most people living with HIV or at risk for HIV do not have access to prevention, care, and treatment, and there is still no cure. However, effective treatment with antiretroviral (ART) drugs can control the virus so that people with HIV can live and feel healthier and reduce the risk of transmitting the virus to the others.

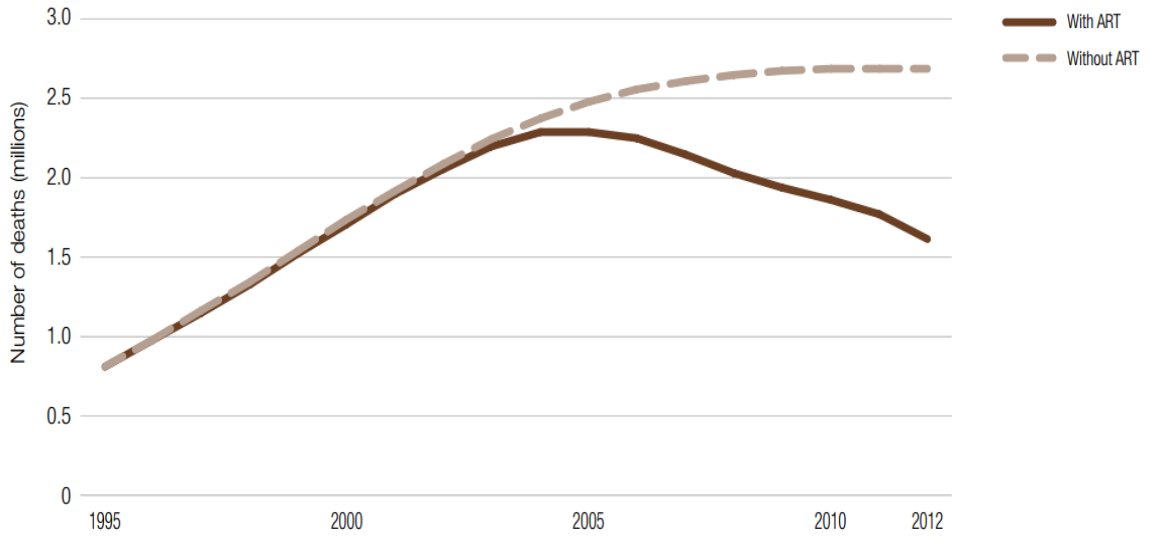

Figure 3: Impact of ART use on the estimated number of deaths due to HIV/AIDS (millions) that would otherwise have occurred in low- and middle-income countries, 1995–2012 (WHO, 2014)

The HIV epidemic not only affects the health of individuals, it impacts households, communities, and the development and economic growth of nations. Many of the countries hardest hit by HIV also suffer from other infectious diseases, food insecurity, and other serious problems. Despite these challenges, there have been successes and promising signs. New global efforts have been mounted to address the epidemic, particularly in the last decade. Prevention has helped to reduce HIV prevalence rates in a small but growing number of countries and new HIV infections are believed to be on the decline. In addition, the number of people with HIV receiving treatment in resource-poor countries has dramatically increased in the past decade. According to WHO, at the end of 2013, 12.9 million people living with HIV were receiving antiretroviral therapy (ART) globally, of which 11.7 million were receiving ART in low- and middle-income countries. About 740,000 of those were children. This is a 5.6 million increase in the number of people receiving ART since 2010. However, almost 22 million other people living with HIV, or 3 of 5 people living with HIV, are still not accessing ART.

Progress has been made in preventing mother-to-child transmission of HIV and keeping mothers alive. According to WHO, in 2013, 67% of pregnant women living with HIV in low- and middle-income countries (970,000 women) received ART to avoid transmission of HIV to their children. This is up from 47% in 2010. (WHO, 2014)

1.1.2. IN TURKEY

Turkey is located between countries of Central Asia and those of Eastern Europe, which have some of the fastest-growing HIV epidemics in the world, (587 new cases in first 6 months in 2013). In spite of its location, Turkey is considered to be at a low level epidemic. The first case of HIV infection was reported in 1985, and by the end of June 2013, the total of 6802 cases had been identified. At the end of the November 2013, the number of case is 7050. The 73% of the HIV positive individual is male. The age distribution showed the most common age of HIV positive people are on age between 40 and 49.

Table 1: Gender distribution of HIV/AIDS cases according to reporting period (1985-2011) (Erbaydar, 2012)

Gender/Years	Female	Male	Number of HIV/AIDS Case
1985-1996	141	476	400
1997-2001	265	443	800
2002-2006	383	836	1200
2007-2011	706	1974	2000

According to the statistics provided by the Ministry of Health (MoH), the main route of transmission is through heterosexual sexual intercourse over 75%) followed by men having sex with men (MSM) at 12% and intravenous drug users (IDU) at 7% among transmission route known cases. Sex work can be considered as a major driver for the epidemic and commercial sex workers form a significant portion of the vulnerable populations. On the other hand, due to IDUs, intravenous drug usage seems to be the second major driver of the epidemic in the future. (MoH, 2013)

Table 2: Age and sex distribution of HIV cases in Turkey. (MoH, June 2013)

Age Range	Male	Female	Unknown Gender	Total
0	19	11	-	30
1-4	15	23	-	38
5-9	11	9	-	20
10-14	10	7	-	17
15-19	50	54	-	104
20-24	410	320	-	730
25-29	733	380	-	1113
30-34	867	325	-	1192
35-39	750	215	-	969
40-49	1090	245	-	1335
50-59	559	153	-	712
60 and >60	275	69	-	344
Unknown Age	138	58	2	198
Total	**4931**	**1869**	**2**	**6802**

As it seen in table 2, the great majority of age distribution is between ages 40 and 49. Secondly the intensity range is between ages 30 and 34.

One year before the ministry of health report, the highest numbers of cases were reported by Erbaydar T. et all, in 20-29 and 30-39 age groups and the number of cases in 40 and over age groups had been increasing. (Erbaydar, 2012)

Table 3: Possible transmission ways of HIV cases distribution in Turkey. (MoH, June 2013)

Transmission Way	Total Case	Percentage %
Heterosexual Relationship	3137	46,1
Homosexual/Bisexual Relationship	670	9.9
Intravenous Drug User	129	1.9
Nosocomial Transmission	109	1.6
Mother To Child	77	1.1
Unknown	2680	39.4
Total	6802	100.0

In 2012; Erbaydar T. et al published a study which is carried out to evaluate the changes in the epidemiological characteristics of HIV / AIDS epidemic in Turkey since 1985. According to this review study, the exclusion of 177 cases which had no data on possible way of transmission, in 57.7% of 440 cases, the way of transmission was reported as heterosexual intercourse. This was the most frequently reported way in 1985-1996 periods. The second transmission way was intravenous drug use (16.1%), the third way of transmission was homosexual-bisexual relationship (14.8%), the fourth was blood transfusion (10.0%), and the fifth was from mother to child transmission (1.4%)

In June 2013, Ministry of Health published a report which has data from 1985 to 2012 June. According to this report, the highest percentage of HIV transmission way is “heterosexual relationship” (46, 1%). The second way of HIV transmission is defined as “unknown” (39, 4%).

1.2. HIV / AIDS

HIV is a retrovirus that infects cells of the immune system, a system composed of lymphocytes and other white blood cells. The lymphocytes are divided into two groups, known as T-cells and B-cells. T-cells are responsible for cellular immunity or fighting off invading antigens, B-cells are responsible for humoral immunity or antibody (immunoglobulin) production. T-cells express different antigens; HIV target T-cells expressing the CD4 antigen (referred to as CD4 cells). HIV integrates itself into the host CD4 cell's DNA and then replicates itself, creating additional virus that ultimately causes the immune cell's destruction and death, which leads to a weakened immune system without enough immune cells to fight infections. (Rockwell, 2011)

HIV is transmitted from person to person through specific body fluids—blood, semen, genital fluids, and breast feeding (mother-child transmission). Having unprotected sex or sharing drug needles with a person who infected by HIV are the most common ways of transition. HIV doesn't spread or transmit by shaking hands, hugging, or closed-mouth kissing with a person who has HIV. And HIV isn't spread through objects such as toilet seats, dishes, or glasses used by a person with HIV. Although it takes many years for symptoms of HIV to develop, a person infected with HIV can spread the disease at any stage of HIV infection. Detecting HIV during the earliest stages of infection and starting treatment well before symptoms of HIV develop can help people with HIV stay healthy. Treatment can also reduce the risk of HIV transmission.

Antiretroviral therapy (ART) is the recommended treatment for HIV infection. ART involves taking a combination (regimen) of three or more anti-HIV medications daily. ART prevents HIV from multiplying and destroying infection-fighting CD4 cells. This helps the body fight off life-threatening infections and cancer. Treatment with anti-HIV medications prevents HIV from multiplying and destroying the immune system. This helps the body fight off life-threatening infections and cancers and prevents HIV from advancing to AIDS. Although it takes many years, without treatment HIV can advance to AIDS. (U.S Department of Health and Human Service, 2012)

Table 4: Centers for Disease Control and Prevention (CDC) Clinical and Immune Cell Categories of HIV Infection

Classification	Categories	Criteria
CD4+ cell count categories	Category 1	≥ 500 cells/microliter
	Category 2	200-499 cells/microliter
	Category 3*	< 200 cells/microliter
Clinical categories	Category A	No symptoms other than persistent generalized lymphadenopathy or those associated with primary HIV infection
	Category B	Symptomatic conditions attributes to HIV of defect in cell-mediated immunity or require management that is complicated by HIV infection
	Category C*	Included diseases that are oppurtinistic and define AIDS

*CD4 Cell Category 3 and Clinical Category C are criteria for the diagnosis of AIDS

To be diagnosed with AIDS, a person infected with HIV must have a CD4 count less than 200 cells/mm^3. (The CD4 count of a healthy person ranges from 500 to 1,200 cells/mm^3. People infected with HIV with CD4 counts less than 500 cells/mm^3 should begin ART.) (U.S Department of Health and Human Service, 2012)

Table 5: Summary Comparison of WHO ART guidelines: immunological criteria for initiating ART, 2010 and 2012

	2010 guidelines	2013 guidelines
adults and adolescents living with HIV	≤ 350 CD4 cells/mm^3	≤ 500 CD4 cells/mm^3
children living with HIV	< 24 months old: all 2-5 years old: ≤750 CD4 cells/mm^3	< 5 years old: all
Pregnant women living with HIV	no specific provision	all
People coinfected with TB and HIV	all	all
People coinfected with Hepatits B and HIV	all with chronic active hepatits	all with chronic severe liver disease
Serodiscordant couples	no specific provision	all

AIDS is an advanced disease caused by acquisition of the human immunodeficiency virus (HIV-1 or HIV-2) and subsequent destruction of the immune system. This decrease in cellular immunity impairs the host's ability to fight off infection and results in the host acquiring opportunistic infections and malignancies. Untreated HIV infection allows for the continued destruction of CD4 cells, resulting in a progression of HIV disease. When the immune system deteriorates to specified and measurable levels, the disease is termed acquired immune deficiency syndrome or AIDS. (Rockwell, 2011)

1.2.1. TESTS and DRUGS

The common HIV test is the HIV antibody test. The HIV antibody test checks for HIV antibodies in a person's blood, urine, or fluids from the mouth.

When a person becomes infected with HIV, the body begins to produce antibodies to HIV. Generally it takes about 3 months to produce enough antibodies to be detected by an HIV antibody test. (For some people, it can take up to 6 months). The time period between infection and the appearance of detectable HIV antibodies is called the window period. Because HIV antibodies are not yet testable, the HIV antibody test is not useful during the window period. The plasma HIV RNA test (also called a viral load test) can detect HIV in a person's blood within 9 days of infection, before the body develops detectable HIV antibodies. The plasma HIV RNA test is recommended when recent infection is very likely—for example, immediately after a person has had unprotected sex with a partner infected with HIV, and especially if the person also has flu-like symptoms.

Detecting HIV at the earliest stage of infection lets people take steps right away to prevent HIV transmission. This is important because immediately after infection the amount of HIV in the body is very high, increasing the risk of HIV transmission. Starting treatment at this earliest stage of infection may also be considered.

To be diagnosed with HIV, a person must have positive results from two HIV tests. The first test may be either an HIV antibody test (using blood, urine, or fluids from the mouth) or a plasma HIV RNA test (using blood). The second test (always using blood) must be a Western blot test. The Western blot test confirms that a person has human immunodeficiency virus. Results of the first antibody test are generally available within a few days. (Rapid HIV antibody tests can produce results within an hour.) Results of the plasma HIV RNA test and Western blot are available in a few days to a few weeks.

When the person has the certain results being HIV positive, need to have drug resistance test. Drug-resistance testing identifies which anti-HIV medications will or will not be effective against a person's strain of HIV.

a. Drug Resistance Test

- HIV drug-resistance testing is recommended in persons with HIV infection at entry into care regardless of whether antiretroviral therapy (ART) will be initiated immediately or deferred **(AII)**. If therapy is deferred, repeat testing should be considered at the time of ART initiation **(CIII)**.
- Genotypic testing is recommended as the preferred resistance testing to guide therapy in antiretroviral (ARV)-naive patients **(AIII)**.
- Standard genotypic drug-resistance testing in ARV-naive persons involves testing for mutations in the reverse transcriptase (RT) and protease (PR) genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern, providers may wish to supplement standard genotypic resistance testing with an INSTI genotype test **(CIII)**.
- HIV drug-resistance testing should be performed to assist in the selection of active drugs when changing ARV regimens in persons with virologic failure and HIV RNA levels >1,000 copies/mL **(AI)**. In persons with HIV RNA levels >500 but <1,000 copies/mL, testing may be unsuccessful but should still be considered **(BII)**.
- Drug-resistance testing should also be performed when managing suboptimal viral load reduction **(AII)**.
- In persons failing INSTI-based regimens, genotypic testing for INSTI resistance should be performed to determine whether to include a drug from this class in subsequent regimens **(AII)**.
- Drug-resistance testing in the setting of virologic failure should be performed while the person is taking prescribed ARV drugs or, if not possible, within 4 weeks after discontinuing therapy **(AII)**. If greater than 4 weeks has lapsed since the ARVs were discontinued, resistance testing may still provide useful information to guide therapy, recognizing that previously selected resistance mutations can be missed **(CIII)**.

- Genotypic testing is recommended as the preferred resistance testing to guide therapy in patients with suboptimal virologic responses or virologic failure while on first or second regimens **(AII)**.
- The addition of phenotypic to genotypic testing is generally preferred for persons with known or suspected complex drug-resistance mutation patterns, particularly to protease inhibitors (PIs) **(BIII)**.
- Genotypic resistance testing is recommended for all pregnant women before initiation of ART **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI)**

Rating of Recommendations: A = Strong; B = Moderate; C = Optional **Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion (Department of Health and Human Services , 2014)

Antiretroviral therapy (ART) is the recommended treatment for HIV. ART involves taking a combination of anti-HIV medications (a regimen) every day.

More than 20 antiretroviral (ARV) drugs in 6 mechanistic classes are Food and Drug Administration (FDA) approved for treatment of HIV infection The six classes are non-nucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs), fusion inhibitors, CCR5 antagonists, and integrate inhibitors.

Recommended HIV treatment regimens include three or more anti-HIV medications from at least two different drug classes. Taking a combination of anti-HIV medications from different classes is the most effective way to control the virus. Some anti-HIV medications are available in combination (two or more medications in one pill). Anti-HIV medications are approved by the U.S. Food and Drug Administration (FDA).

HIV positive people generally receive a combination of antiretroviral drugs because a single patient may have several different strains (types) of the virus circulating in the blood. The different strains of the virus may respond differently to specific types of drugs. Therefore, highly active antiretroviral therapy (HAART), which is a combination of drugs from at least two different classes, is recommended.

There are six major types of drugs used to treat HIV/AIDS. Called antiretroviral because they act against the retrovirus HIV, these drugs are grouped by how they interfere with steps in HIV replication.

1. Protease Inhibitors (PIs)

Use of HIV PIs has been associated with hyperlipidemia that is more common and more severe than what was observed before the advent of HAART.

All protease inhibitors (PIs) are metabolized in the liver by CYP3A isoenzymes; consequently their metabolic rates may be altered in the presence of CYP inducers or inhibitors. Co-administration of PIs with ritonavir (RTV), a potent CYP3A inhibitor, intentionally increases PI exposure. The list of drugs that may have significant interactions with PIs is extensive and is continuously expanding. Some examples of these drugs include lipid-lowering agents (e.g., statins), benzodiazepines, calcium channel blockers, immunosuppressants (e.g., cyclosporine, tacrolimus), anticonvulsants, rifamycins, erectile dysfunction agents (e.g., sildenafil), ergot derivatives, azole antifungals, macrolides, oral contraceptives, methadone, and HCV protease inhibitors. Herbal products, such as St. John's work, can also cause interactions that increase the risk of adverse clinical effects. (Department of Health and Human Services , 2014)

There are some studies which have done by Dube et al;
Sixty-two (47%) of 133 PI recipients at one clinic had lipid abnormalities that met the 1994 NCEP intervention criteria. In the Swiss HIV Cohort, hypercholesterolemia and hypertriglyceridemia were 1.7–2.3 times more common among individuals receiving HAART that contained a PI.
Hypercholesterolemia (cholesterol level, 1240 mg/dL) and severe hypertriglyceridemia (triglyceride level, 1500 mg/dL) occurred in 60% and 75% of subjects, respectively, receiving HIV PIs at one center, with respective incident dyslipidemia rate ratios of 2.8 and 6.1 attributable to use of these medications.
The dyslipidemia associated with use of HIV PIs often includes hypercholesterolemia. Much of the increase is in the level of very-low density lipoproteins (VLDLs) and, to a lesser extent, intermediate-density lipoproteins (IDLs). HDL-C levels tend not to change or to increase. Inconsistent changes in small and large HDL particles have

been described. Increased LDL-C levels have been reported in some studies but not others. Compared with patients receiving lamivudine- based antiretroviral therapy, PI recipients had a mean increase in the total cholesterol level of 32 mg/dL at a mean of 3.4 months of therapy, which included a 27% increase (18 mg/dL) in the directly measured LDL-C level.

Hypertriglyceridemia is also common and appears to be especially severe in patients taking ritonavir. Increased triglyceride concentrations have been found in all lipoprotein fractions and are accompanied by hyper apobetalipoproteinemia, which is associated with an increased risk of vascular events. Lipoprotein(a) excess has been described inconsistently, but it may be exacerbated in individuals with this disorder before HAART initiation. (Dube, 2003)

2. Entry Inhibitors interfere with the virus' ability to bind to receptors on the outer surface of the cell it tries to enter. When receptor binding fails, HIV cannot infect the cell.

3. Fusion Inhibitors interfere with the virus's ability to fuse with a cellular membrane, preventing HIV from entering a cell**.**

4. Reverse Transcriptase Inhibitors prevent the HIV enzyme reverse transcriptase (RT) from converting single-stranded HIV RNA into double-stranded HIV DNA—a process called reverse transcription. There are two types of RT inhibitors:

- Nucleoside/nucleotide RT inhibitors (NRTIs) are faulty DNA building blocks. When one of these faulty building blocks is added to a growing HIV DNA chain, no further correct DNA building blocks can be added on, halting HIV DNA synthesis.
- Non-nucleoside RT inhibitors (NNRTIs) bind to RT, interfering with its ability to convert HIV RNA into HIV DNA

5. Integrase Inhibitors block the HIV enzyme integrase, which the virus uses to integrate its genetic material into the DNA of the cell it has infected**.**

6. Multi-class Combination Products combine HIV drugs from two or more classes, or types, into a single product.

To prevent strains of HIV from becoming resistant to a type of antiretroviral drug, healthcare providers recommend that people infected with HIV take a combination of antiretroviral drugs in an approach called highly active antiretroviral therapy (HAART). Developed by NIAID-supported researchers, HAART combines drugs from at least two different classes.(FDA)

The best combination of anti-HIV medications depends on individual's needs. Factors that person and person's health care provider will consider when selecting HIV regimen include:

- Other diseases or conditions people may have
- Possible side effects of anti-HIV medications
- How anti-HIV medications may interact with other medications people take
- The drug-resistance testing results
- Complexity of the regimen—how many pills to take every day and how often, and if pills must be taken with or without food
- Any personal issues that may make following a regimen difficult (such as depression or alcohol or drug abuse)

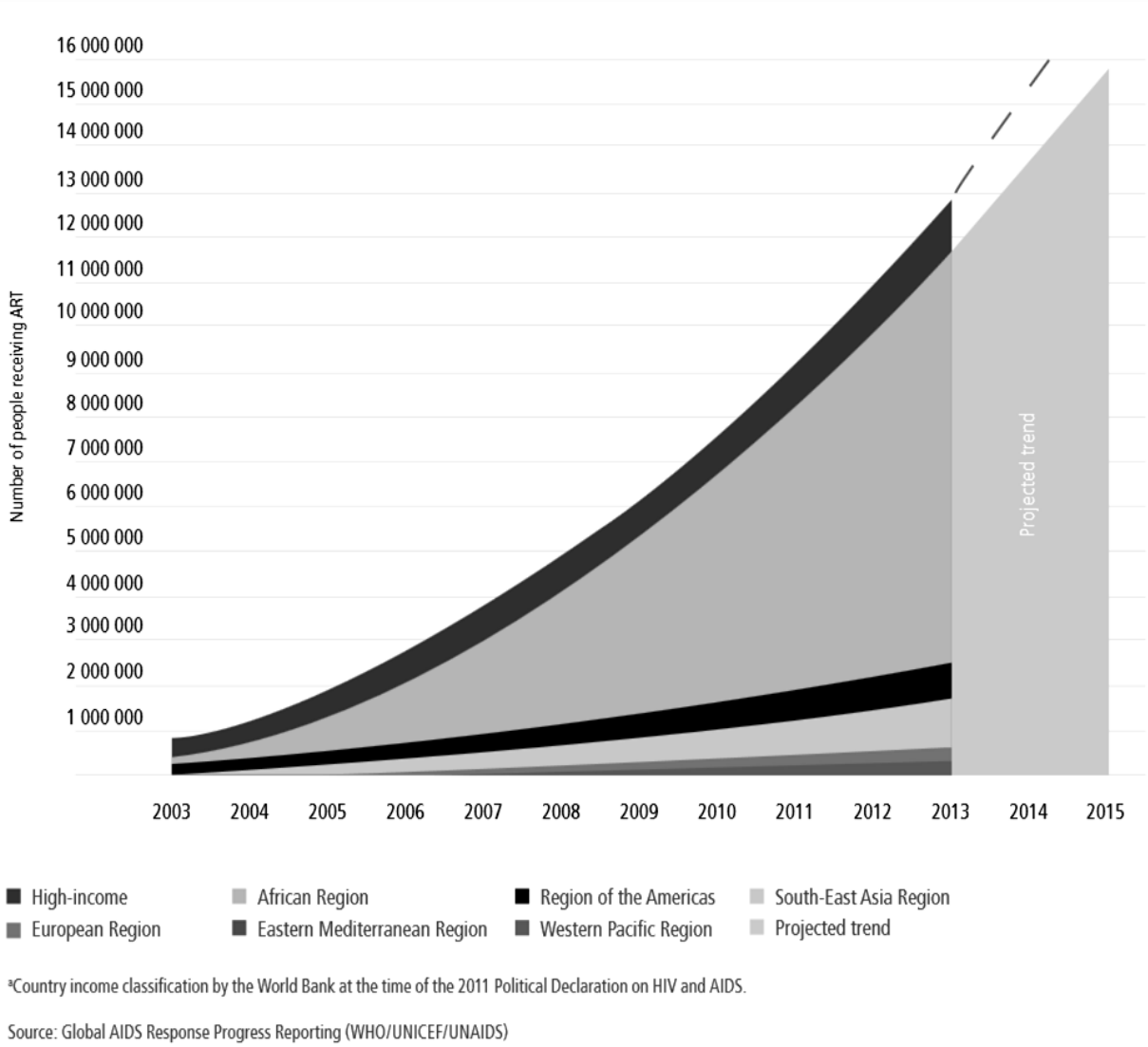

Figure 4: the number of people receiving ART according to the income in 2003-2015

The health care provider will use two important tests to monitor the treatment regimen: CD4 count and viral load test. Both tests are done using a sample of blood. The results of the tests will help the health care provider determine if the anti-HIV medications in patient's regimen are working.

HIV attacks the immune system, destroying the system's infection-fighting CD4 cells. Keeping the immune system healthy is an important goal of HIV treatment. The CD4 count measures the number of CD4 cells in a sample of blood. Because a falling CD4 count is a sign that HIV is damaging the immune system, the test is a key factor in deciding when to start treatment. The CD4 count is also used to monitor how well treatment is working.

The CD4 count of a healthy person ranges from 500 to 1,200 cells/mm^3. HIV-infected people with a CD4 count less than 500 cells/mm^3 should begin taking anti-HIV medications. An HIV-infected person with a CD4 count less than 200 cells/mm^3 has AIDS. Once patient start treatment, he/she should have a CD4 count once every 3 to 4 months. An increasing CD4 count is a sign that the treatment regimen is working. If the regimen is working well, he/she needs a CD4 count only once every 6 to 12 months.

Preventing HIV from multiplying is another important goal of HIV treatment. The viral load test measures the amount of HIV in the blood. It's the best measure of how well the treatment regimen is controlling the virus.

The best sign that treatment is working is achieving and maintaining an undetectable viral load. An undetectable viral load doesn't mean that patient's cured. It means that the amount of HIV in the blood is too low to be detected by the viral load test. Once the patient starts treatment, he/she should has a viral load test within 2 to 8 weeks, and then once every 4 to 8 weeks until the viral load is undetectable. The patient needs the test done only every 3 to 4 months once the viral load is undetectable. If the patient has an undetectable viral load for more than 2 or 3 years, patient's health care provider may recommend viral load testing once every 6 months.

HIV treatment regimens can fail for a variety of reasons, including:

- Side effects from anti-HIV medications: Unpleasant side effects, such as fatigue, nausea, and diarrhea, can make treatment adherence difficult. Severe side effects make it impossible to safely follow a regimen.

- Poor absorption of anti-HIV medications to work effectively, anti-HIV medications must be absorbed by the body.

- Drug interactions: Drug interactions between anti-HIV medications and other medications can increase the risk of side effects. Drug interactions can also reduce the effectiveness of anti-HIV medications. (Anti-HIV medications can also have the same effects on other medications.)

- Drug resistance: Drug resistance occurs when HIV mutates (changes form), causing one or more medications in a regimen to be ineffective.

• Poor treatment adherence: Skipping medications gives HIV the chance to multiply, increasing a person's viral load. Poor adherence also increases the risk of drug resistance. (U.S Department of Health and Human Service, 2012)

The person who lives with HIV should know that the most tests should be repeat during the life. Table 6 explains the tests and the period of repeating.

Table 6: Laboratory Monitoring Schedule for HIV-Infected Patients Before and After Initiation of Antiretroviral Therapy (U.S. Department of Health and Human Services, 2015)

Lab Test	Follow Up Before Initiation of ART	ART Initiation or Modification	Follow-Up 2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months
CD4 Count	Every 3–6 months	+		During first 2 years of ART or if viremia develops while patient on ART or CD4 count	After 2 years on ART with consistentl y suppressed viral load: CD4 Count 300– 500 cells/mm3 : • Every 12 months CD4 Count >500 cells/mm3 : • CD4 monitoring	+
HIV Viral Load	Repeat testing is optional		+			
Resistance Test	+	+				
Basic Chemistry	Every 6–12 months	+		+		

ALT, AST, T. bilirubin	Every 6–12 months	+		+		
Fasting Lipid Profile	If normal, annually		Consider 4–8 weeks after starting new ART regimen that affects lipids	If abnormal at last measurement	If normal at last measurement	
Fasting Glucose or Hemoglobin A1C	If normal, annually			f abnormal at last measurement		If normal at last measurement

1.2.2. Impact Of ART On Dietary Intake And Nutritional Status

One of the most important observations about the interaction between ART and nutritional status is that initiating ART often leads to a reversal of symptoms caused by HIV such as malnutrition and loss of body mass (including muscle mass). Increased appetite, improved food intake and reduced viral load improve nutritional status. This improvement is associated with a reduction in morbidity and mortality from HIV related causes.

There are a number of food interactions that influence not only the absorption and utilization of ART but also impact on digestion, absorption and assimilation. It is also known that certain antiretroviral therapies can produce a range of side effects and metabolic complications that have a significant impact on health and wellbeing. Some of the more common side effects include diarrhoea, loss of appetite, bloating, and nausea and unexplained weight change. There is a growing amount of evidence about the long term complications of ART in a significant proportion of adults, children and infants living with HIV. These metabolic complications include disorders such as lipodystrophy, dyslipidaemia, and insulin resistance, abnormalities in glucose tolerance, lactic acidosis, mitochondrial toxicity, and bone demineralization. It appears that these complications may be related to particular drugs. These side effects may have serious consequence in terms of adherence with ART, increased risk of chronic diseases including cardiovascular disease and diabetes, and reduced

quality of life. These metabolic effects not only impact on the health and wellbeing of PLHIV but may necessitate a shift t another ART regime. (Houtzager, 2009)

Despite advances in the knowledge about interactions between ART and nutritional status, many questions remain unanswered. The consequences and efficacy of ART among individuals with pre-existing (primary) malnutrition are unclear. The effects of underlying malnutrition on the absorption and metabolism of all or individual ART medication are not fully understood. It is also unclear whether nutritional supplementation can prevent or reduce the occurrence of complications or side effects due to ART.

Among infants and children, the impact of acute or chronic severe malnutrition on immune function and response to ART, including experience of side effects is not well understood. Further research and monitoring is also required to elucidate the impact ART has on growth among infants and children, particularly from resource poor settings.

In many parts of the world, supplementation using herbal and alternative therapies is a common practice for many PLHIV. Although the effects of these supplements are becoming clearer there is still much that needs to be learned about the interactions between ART medication and various traditional therapies. (Houtzager, 2009)

1.3. HIV and Nutrition

Nutritional disorders are often present in HIV/AIDS patients. Good nutrition plays a vital role in the immune system of all people, including (PLHIV). It strengthens the immune system, while HIV infection and poor nutrition have a cumulative effect in damaging it. PLHIV are more vulnerable to malnutrition than the general population and nutritional status is a good predictor of their mortality risk. (Grobler L, 2013)

Adequate nutrition is critical for optimal immune function. Dietary therapy is therefore regarded as an important adjunct in the clinical care of patients infected with HIV. It is believed that achieving and maintaining optimal nutrition will improve the individual's immune function, reduce the incidence of complications associated with HIV infection, attenuate the progression of HIV infection, improve quality of life, and ultimately reduce mortality associated with the disease.

People living with HIV are at great risk of nutritional disorders. This is the case in both untreated (i.e. not receiving antiretroviral therapy (ART)) and treated (i.e. receiving some form of ART) HIV-infected individuals. Furthermore, HIV infection is most prevalent in parts of the world where food security is compromised. Populations at high risk of HIV infection may lack appropriate nourishment prior to infection by HIV. Starvation and undernourishment severely compromise the immune system thereby increasing both susceptibility to HIV infection and progression of HIV/AIDS. (Grobler L, 2013)

Untreated HIV infection is characterized by increased resting energy expenditure, decreased appetite, decreased intake and digestion of food and decreased absorption of nutrients (Koethe, 2010).

HIV-infected individuals receiving antiretroviral therapy may experience the adverse effects of antiretroviral drugs such as nausea and insomnia, which also have a negative impact on nutrient status. Poor nutrient status may in turn exacerbate these adverse effects, in part by increased drug toxicity.

Total daily energy expenditure (TDEE) has three components: Resting energy expenditure (REE) or resting metabolic rate (RMR), physical activity (PA) and diet-induced thermogenesis in adults and an additional allowance for growth in children. Diet-induced thermogenesis takes 5-10% of TDEE. Digestion and assimilation of foods are included. Physical energy expenditure takes 20% of TDEE and it is variable. The different components of TDEE can vary between each other. Thus, while RMR is often increased in HIV/AIDS TDEE does not necessarily increase because physical activity may be reduced because the patient feels too ill to get up and work. Indeed TDEE was decreased among men with HIV/AIDS during rapid weight loss, mainly because physical activity was reduced. TDEE studies have not been performed in HIV-infected children. However, ill children are usually less active and have a poor appetite so a lower TDEE might be expected in pediatric HIV/AIDS. TDEE is therefore not a major explanatory factor for energy imbalance in patients with HIV/AIDS. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

While explaining the TDEE, RMR and REE are used at the same time. Both BMR, and RMR, estimates the number of calories burned at rest, but RMR takes additional

factors into consideration when determining needs. BMR measures the basal energy expenditure, or BEE. The BEE is a 24 hour estimation of the number of calories body burns maintaining the most basic bodily functions, such as breathing, circulating blood and growing and repairing cells. RMR measures the resting energy expenditure. REE determines the number of calories body burns in a 24 hour period maintaining basic bodily functions, but also includes the number of calories burned eating and conducting small amounts of activity.

REE takes 60-70% of TDEE. It includes bodily functions and lean body mass belongs to REE. As with many infections increased resting metabolic rate (RMR) is often suggested as an important factor for energy imbalance in HIV/AIDS. There are differences in energy expenditure between children and adults with HIVAIDS. Most studies in adult patients show that RMR is around 10% higher than in control groups. RMR is highest in those with the most severe disease. In particular those with secondary infection had higher RMRs than did patients without secondary infection. Unlike adults, most studies in children show no difference in RMR between infected and uninfected children, though studies do show raised energy expenditure in children with opportunistic infections. The different results in children and adults may be due to differences in nutritional status, dietary intake or disease severity. It is important to recognize that the effects of energy imbalance is more serious in children than adults because a high proportion of energy is required for growth in healthy children and for catch up growth by children recovering from an opportunistic infection . Thus, despite the generally consistent finding that RMR is increased by 10% among adults with HIV/AIDS, change in RMR alone does not account for weight loss in adults and hardly contributes to weight loss in children. Other factors that contribute to total daily energy expenditure (TDEE) include physical activity, growth and diet-induced thermogenesis; these are not taken into account in measurement of RMR. Variations in results of measurements of energy expenditure are likely due to differences in dietary intake, nutritional status, physical activity, and severity of opportunistic infection. However overall RMR is increased by about 10% in HIV/AIDS and is especially high during acute severe episodes of opportunistic infection. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

As a result of the increased REE in untreated HIV infection, both fat and protein stores are oxidized to fuel the body’s energy requirements. (Macallan, 1995a) Whole-

body protein turnover is up to 25% higher in untreated HIV-infected individuals than in HIV-negative controls (Macallan, 1995b) and fat stores are replenished more readily than protein stores even when nutrition is adequate. The resultant loss of body protein could further compromise the immune system of the HIV-infected individual. HIV-associated weight loss and wasting are independent contributing factors to poor clinical outcomes in people living with HIV/AIDS. In most cases, acute weight-loss episodes are associated with secondary infections. Once the secondary infections are successfully treated and energy intake is increased sufficiently, patients are able to regain weight and remain weight-stable. Instances of chronic weight loss are normally associated with secondary gastrointestinal infections and subsequent malabsorption. (Grobler L, 2013)

Weight loss and low Body Mass Index (BMI < 17kg.m−2), a proxy for poor nutritional status, are independent predictors of mortality, particularly in resource-limited settings (Liu, 2011). This remains true despite the introduction of ART. In a recent study, Liu 2011 found that HIV-infected patients with low BMI (BMI<17kg.m−2) had a significantly higher risk of early mortality (death within 3 months) following the initiation of ART. Of the patients who survived the first 3 months of ART, those who experienced weight loss had a higher risk of subsequent death compared to those who were weight stable during this period. (Grobler L, 2013)

1.3.1. Malnutrition

It is not always possible to identify one single cause as the main contributor to declining nutritional status or malnutrition in HIV. Primary and secondary malnutrition may exist together in PLHIV worsening the effect on health. Primary malnutrition is caused by inadequate consumption of food and essential nutrients due to: food not being available or accessible; or poor eating habits. Secondary malnutrition results from infection or disease, leading to increased energy expenditure, malabsorption or altered utilization of nutrients. (Houtzager, 2009)

“Cachexia” describes a preferential loss of LBM, which implies metabolic derangement rather than a nutrient deficiency. “Wasting” is a less precise term that suggests weight loss due to inadequate nutrient intake. The term has also been used for severe weight loss, but the exact point at which progressive weight loss becomes wasting is problematic. (Mangili, 2006)

Table 7: Suggested Criteria for the Diagnosis of Wasting in HIV Disease

Suggested Criteria for the Diagnosis of Wasting in HIV Disease	
Parameter	**Criteria**
Weight Loss	10% loss over 12 months
	7,5% loss over 7 months
Body Mass Index	< 20%
Body Cell Mass	5% loss over 6 months
	35% of weight if BMI is less than 27 in men
	23% of weight if BMI is less than 27 in women

* (Polsky B., 2001)

Poor nutrition status may be caused by many different factors. Decreased caloric intake, malabsorption of nutrients/nutrient losses, metabolic changes/increased energy expenditure during secondary bacterial or systemic opportunistic infections contribute to malnutrition in these patients. (J. Salamon, 2002) Oxidative stress, hormonal abnormalities, HAART treatments, psychosocial difficulties may be the other causes of malnutrition. (Marcie, 2000) (Colecraft, 2008)

Untreated HIV infection causes increased REE, decreased appetite and intake of food and it causes the decreased digestion functions. It all means that the nutrient absorption is decreased. Loss of appetite leading to reduced energy intake is the main reason why people lose weight in HIV/AIDS

Malnutrition occurs primarily while the consumption of essential nutrients is inadequate. Secondarily, the opportunistic infections increased resting energy expenditure and malabsorption causes the malnutrition.

a) Inadequate food intake

HIV is associated with biological factors such as loss of appetite, gastrointestinal complications and oral and oesophageal sores that affect the individual's desire for food and ability to eat, leading to inadequate dietary intakes. In developing countries these biological effects are exacerbated by the social consequences of the disease, which typically culminate in food insecurity. Households affected by HIV/AIDS confront severe declines in the availability of food (both quantity and quality) because

of a decrease or complete loss of the socio-economic contributions of sick household member(s) as well as their caregivers. Lack of social support as a result of stigmatization and discrimination also contributes to reduced food availability and hence inadequate dietary intakes by those affected by HIV. (Colecraft, 2008)

Loss of appetite leading to reduced food intake (and nutrients) is one of the main reasons why people lose weight with HIV infection. Reduction in dietary intake may lead to growth failure in HIV-positive children and wasting in HIV-positive adults. Inadequate food intake prevents recovery from malnutrition. Inadequate food intake is caused by many different factors. In addition to lack of food, the desire to eat may be reduced in PLHIV by various factors, including but not limited to:

- Oral candidiasis (OR), mouth or gastrointestinal tract ulceration/irritation making eating and swallowing uncomfortable.
- Infections resulting in reduced appetite, nausea, vomiting and/or diarrhoea.
- Metabolic effects of malnutrition, diarrhoea and drugs.
- Psychosocial factors including depression and lack of emotional support.
- Antiretroviral side effects such as nausea and diarrhea. (Houtzager, 2009)

b) Increased energy expenditure

PLHIV have a resting metabolic rate (RMR) that is around 10% higher compared to HIV negative adults, and this 20-30% higher when they have secondary or opportunistic infections. Increased energy expenditure will often lead to weight loss in PLHIV. This weight loss may occur despite an individual maintaining their usual food intake after acquiring HIV, and during all stages of the disease. (Houtzager, 2009)
Antiretroviral therapy (ART) blocks the replication of HIV and metabolism returns back to almost normal. All enzymes and cell structures need to be re-synthesized, which requires 20% increase in basic energy expenditure, amount of substrates and microelements. Clinical manifestations of beriberi disease and other hypovitaminoses can be prevented by multivitamin supplementation, especially thiamine in high doses, intravenously when necessary. Again WHO stresses that the available data lack scientific merit. However proper nutrition, especially high fiber diet, can help to improve ART adherence and decrease rate of side effects. Also vitamin E, C and B supplements improve immune function by increasing number of circulating CD4 cells

and decreasing viral load. It has been proven that antioxidants can decrease HIV viral load considerably even in the absence of ART. They seem to decrease inflammation, nuclear factor kappa B (NfkB) concentration as well as HIV's rate of transcription by swiping free radicals.

Immunomodulatory nutrients (alanyl-glutamine, L-carnitine and omega-fatty acids) which have positive effects on immune function in surgery or oncology patients, turned out to be of no value in HIV/AIDS patients. All other oral nutrition formulae are comparable. (Szetela, 2012)

In 1999, Sharbet et al. described common sense suggestions on possible dietetic interventions in the following clinical situations:

- Fever and lack of appetite: High calorie, high protein, tasty foods, juices, small but frequent meals. Routine three daily meals should be accompanied by small bites 15-30 times a day to help arrive at the required daily food intake.
- Oral cavity pain: High calorie and high protein meals to provide for basic requirements. Avoid sour and sweet foods. Meals should be dense and in room temperature. (Szetela, 2012)

Oral health conditions also affect up to 90% of PLHIV at some time during the course of their disease. Oral lesions may be associated with a variety of infectious, neoplastic or inflammatory conditions. Oral candidiasis (OC) occurs frequently in PLHIV and usually presents as white or yellow plaques on the roof of the mouth, tongue and inside cheeks. The incidence and severity of OC increases as the CD4 count decreases. Oropharyngeal

candidiaisis is more common in patients with CD4 counts <200 cells/µl.

Mouth infections including candidiasis can alter taste and reduce appetite. Painful lesions in the mouth, throat and oesophagus contribute significantly to the reduction in food and liquid intake in PLHIV and warrant aggressive investigation and management where possible.

Treatment of candidiasis in PLHIV includes topical agents where oral disease is mild (eg nystatin emulsion, Miconazole gel or amphotricin lozenges), and systemic treatment with Fluconazole or Itraconazole for more severe disease. There are no particular foods which affect recovery from candidiasis or ulceration although ulcerated lesions are usually more sensitive to salty, spicy and acidic agents. Eating a healthy diet is important for good health, though often food intake is reduced due to

mouth soreness or painful swallowing. Modifying the texture and type of foods can help ensure adequate food intake. (Houtzager, 2009)

- Nausea and vomiting: Dry meals flat in taste, small and frequent.
- Irritable colon: Small, frequent and dense meals, bananas, rice and porridge. Avoid dairy products and fatty foods.
- Chronic fatigue syndrome: High calorie, colourful and tasty foods. Preserve energy during day; get help preparing meals and reserve time to eat.
- Diarrhoea: Bananas, rice and porridge. Supplement fluids and electrolytes. (Szetela, 2012)

Diarrhoea is one of the most common symptoms experienced by PLHIV. Diarrhoea is the passage of 3 or more loose or liquid stools per day, or more frequently than is normal for the individual. The causes of diarrhoea will vary depending on an individual's immune status. Parasites, bacteria and viruses may account for up to 80% of diarrhoea experienced by PLHIV. Medications, including ART, may also cause or exacerbate diarrhoea in PLHIV. Diarrhoea is a symptom. When possible, the underlying cause of diarrhoea should be identified and treated. In some instances symptomatic treatment alone may be adequate or all that is available but in most cases investigation is preferable to determine the cause prior to medical intervention. Symptom control strategies include dietary modification, fluid and electrolyte replacement (eg an oral rehydration solution of ½ tsp of salt, 8 tsp of sugar to 1L of boiled water) and anti-diarrheas. These are often necessary in addition to further medical interventions, particularly in cases of moderate to severe diarrhoea in PLHIV. (Houtzager, 2009)

One clinical trial, which assessed the effect of dietary modifications on HIV, related diarrhea using normal foods (ie non supplemental) showed a significant reduction in stool frequency and consistency. The intervention diet included 50% reduction in intake of fat, lactose and insoluble fiber, 50% increase in soluble fiber and the elimination of caffeine. These dietary modifications resulted in a 28% reduction in stool frequency in the treatment groups vs. 15% in the controls. Stool consistency improved 20 % in the treatment group vs. 8% in the controls.

c) Energy malabsorption

Intestinal malabsorption leading to nutrient energy loss, is common in patient with HIV/AIDS. Chronic weight loss in HIV/AIDS often related to gastrointestinal disease and malabsorption. In addition to the damage to the intestinal villi caused by HIV, Cryptosporidium, one of the commoner and more serious opportunistic gut infections, for example, causes malabsorption and the degree of intestinal injury is related to the number of organisms infecting the intestine. Several studies have shown that those with more severe malabsorption have lower body mass index. Fast small bowel transit time. Children with HIV/AIDS can have devastating severity of diarrhoea, making it almost impossible to keep pace with rehydration therapy. Possible mechanisms responsible for malabsorption in HIV/AIDS include the impact of HIV on villi, specific enzyme deficiencies in intestinal mucosa, the effect of opportunistic infections and altered intestinal transit have all been considered but these are mainly conjectural and effective treatments remain to be developed. The impact of nutritional interventions which are known to improve diarrhoea and nutrient absorption in non-HIV populations such as zinc, have not been evaluated in children HIV/AIDS but rather disappointing results were achieved in adults. Albendazole appears to improve absorption but the mechanisms are unclear. Carbohydrate malabsorption occurs in children with HIV/AIDS, even in those without bacterial or protozoal pathogens. High levels of fecal fat occur; one study showed that over 90% of HIV-positive patients had high faecal fat levels that were not related to dietary fat intake. Over 80% of HIV positive patients in one study had faecal fat levels in the range of 20–30% of dietary fat intake.

With these high levels of fat malabsorption, a negative energy balance will develop unless there is considerable increase in dietary energy. Fat malabsorption may be improved by use of pancreatic enzyme supplements. One study showed benefits from probiotics. Carbohydrate malabsorption is especially severe among children with immune depression. Malabsorption of iron also occurs. Despite the well documented evidence of fat malabsorption in HIV/AIDS it is possible to achieve nutritional rehabilitation using high fat diets, though whether alteration sin the fat content of rehabilitation diets in severely malnourished children has not been

investigated. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

1.4 Nutrient Requirements:

1.4.1 Energy Requirements

Table 8: Energy requirement table for HIV positive people

Population	Asymptomatic	Symptomatic
Adults	10%	20-30%
Pregnant/Lactating women	10%*	20-30%*
Children	%10	with no weight loss: 20-30% with weight loss: 50-100%

*In addition th the extra energy requirements due to HIV infection, it is important to keep in mind that pregnant and lactating women need to consume extra energy and micronutrients required by pregnancy or lactation. (USAID, 2007)

a. Adults:

Studies point to low energy intake combined with increased energy demands due to HIV infection and related infections as the major driving forces behind HIV-related weight loss and wasting. Based on increased resting energy expenditure (REE) observed in studies of HIV-infected adults, it is recommended that energy be increased by 10% over accepted levels for otherwise healthy people. The goal is to maintain body weight in asymptomatic HIV-infected adults. Although studies of energy expenditure have not shown an increase in total energy expenditure (TEE), this may have been the result of individuals compensating by reducing activity-related energy expenditure (AEE). Since maintaining physical activity is highly desirable for preserving quality of life and maintaining muscle tissue, it is undesirable that energy intake should only match a reduced level of AEE. The estimated energy requirement therefore allows for normal AEE levels on top of an increased level of REE. Increased energy intake of about 20% to 30% is recommended for adults during periods of symptomatic disease or opportunistic infection to maintain body weight.

This takes into account the increase in REE with HIV-related infections. However, such intakes may not be achievable during periods of acute infection or illness, and it has not been proven that such high intake levels can be safely achieved during such periods.

Moreover, it is recognized that physical activity may be reduced during HIV-related infections and the recommended increased intake is based on the energy needed to support weight recovery during and after HIV related illnesses. Intakes should therefore be increased to the extent possible during the recovery phase, aiming for the maximum achievable up to 30% above normal intake during the acute phase. (WHO, 2003)

b. Children

There are few studies on energy expenditure in HIV-infected children. Energy requirements in children can vary according to the type and duration of HIV-related infections, and whether there is weight loss along with acute infection. Although the finding of increased resting energy expenditure in asymptomatic disease has not been replicated in children, similar to asymptomatic HIV-infected adults an average increase of 10% of energy intake is recommended to maintain growth. Based on clinical experience and existing guidelines to achieve catch-up growth in children irrespective of HIV status, energy intakes for HIV-infected children experiencing weight loss need to be increased by 50% to 100% over established requirements for otherwise healthy uninfected children. (WHO, 2003)

Evidence to support specific recommendations for managing severe malnutrition in HIV-infected children is not yet available. In the absence of specific data with regard to HIV infection, existing WHO guidelines1 should be followed. Research is needed on the specific energy requirements of HIV-infected children. (WHO, 2003)

c. Pregnant and Lactating Women

At present, there are no specific data on the impact of HIV/AIDS and related conditions on energy needs during pregnancy and lactation over and above those requirements already identified for non-infected women. For now, the recommended

energy intake for HIV-infected adults should also apply to pregnant and lactating HIV-infected women. (WHO, 2003)

Stack et al reported that, in most cases of undernutrition simple interventions are usually enough. Only when cachexia or wasting develops, is it necessary to consult nutritional therapist or anesthetists who might then start intravenous or PEG (Percutaneous Endoscopic Gastrostomy) nutrition. Intravenous nutrition can help supplement amino acids, fatty acids, glucose and microelements but it does not lead to substantial increases in lean body mass. Oral food intake and physical exercise should be start as soon as possible. (Szetela, 2012)

1.4.2. Protein Requirements

Protein deficiency is closely associated with energy deficiency; both are often deficient in HIV/AIDS and there is so much evidence of severe protein deficiency in HIV/AIDS that it is has been proposed that children and adults with HIV/AIDS need much more protein than in their uninfected peer. Establishing the amount of protein which an individual needs to maintain body composition and function and, in the case of children, to grow is difficult. Most studies have examined the metabolism of individual labeled amino acids as they become incorporated into pools of body protein or excreted as metabolic products. At the end, it is always questioned that the HIV-positive individuals should need to eat more protein or not. On the other hand, it is also questioned that the HIV positive individual need a different proportion of protein in their diet or not. A clinical state of protein depletion suggests that greater amounts of dietary protein are required. However, much evidence from animal and human studies models in septic or catabolic states similar to HIV/AIDS shows that increased levels of amino acid or protein intake are not utilized adequately. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

Several pro-inflammatory cytokines are produced during infection, which results in poor appetite and failure to grow or regain lost weight even when abundant nutrient supplies are provided. There are informative examples of abnormal protein metabolism in infected children and adults. Several of these have involved providing considerable amounts of protein. Increasing dietary intake surely changes protein

metabolism and the balance between anabolism and catabolism but it does not appear that overall additional protein intake can replace lost protein stores until the infection is better managed. So, provision of additional protein does not in any way guarantee increased lean body mass and recovery of blood protein levels. Indeed, clinical status can deteriorate if hyper alimentation (hyper alimentation: administration or consumption of nutrients beyond minimum normal requirements, in an attempt to replace nutritional deficiencies.) is given in the presence of sepsis. Although weight gain often occurs in HIV-positive patients with active opportunistic infection who are treated with total parenteral nutrition, body composition analysis showed that the weight gained was predominantly fat. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005). It explains a lot about eating more protein is necessary or not.

Administration of excess dietary amino acids requires disposal processes including deamination and oxidation; these processes themselves require more energy. The utilization of certain essential cellular cofactors may be deleterious to host metabolism. Thus modern nutritional support regimens for patients with sepsis tend to avoid hyperalimentation until the infection has been controlled. Direct evidence for specific clinical benefit from known increments of protein intake is largely lacking and will depend on the nutritional and inflammatory state of the patient. Dietary protein intake is often reduced in HIV/AIDS, especially during opportunistic infection; it is difficult to overcome this dietary reduction and doing so in the presence of opportunistic infection can be harmful. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

According to the WHO, there are insufficient data at present to support an increase in protein intake for PLWHA above normal requirements for health i.e. 12% to 15% of total energy intake. (WHO, 2003)

Position of the American Dietetic Association and Dietitians of Canada also reported the nutrient requirements of HIV infected people. HIV infected patients require on average 1.2 g/kg/day protein however, if infection is uncontrolled, the requirement increases by %33 to 1.8g/kg/day protein. Basic energy consumption increases by 8-15% in chronically HIV infected individuals, by 20-30% in AIDS patients and 30% if

opportunistic infections develop. Thus both protein and energy requirements have to be adjusted accordingly. (Szetela, 2012)

a. Protein metabolism

Body protein loss is due to poor dietary intake, malabsorption and metabolic change. As we know, in the absence of adequate energy intake, body fat and protein are used as fuel sources, thus energy and protein metabolism cannot be separated within the context of clinical HIV/AIDS. During weight loss in HIV/AIDS the proportion of body stores that are lost, be they protein, fat or carbohydrate depends on the underlying nutritional state and the dietary intake. Thus the initial level of body protein and fat, together with the dietary intake and the rate of weight loss will be affected by the severity of the inflammatory response. The proportion of loss of each compartment changes according to the individuals' genetic differences. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

Fat is usually lost first and as body fat stores become progressively depleted, more lean body mass is lost per kilogram of total weight loss. The overall result is that protein depletion becomes more striking once fat reserves are lost. These changes are widely described in many wasting illnesses, but HIV seems to induce a special metabolic effect in the host involving a preferential loss of protein over fat. Evidence for preferential protein depletion in HIV comes largely from many cross-sectional studies about body composition in which patients with AIDS wasting have been found to have proportionately greater loss of lean mass than fat. Patients with HIV/AIDS experience frequent experience episodes of clinical infection from repeated opportunistic pathogens infections, in between which they can rebuild nutrient stores.

Repeated episodes of weight loss due to loss of fat and lean tissue followed by recovery appear to allow fat to be preferentially repleted and thus measurement of weight gain without assessment of body composition may lull clinician into a false sense of security. Indeed preferential fat repletion occurs elsewhere – in post starvation refeeding, in TB and in some severely malnourished children where they deposited more fat than protein if they were zinc deficient. Preferential fat deposition was also noted during nutritional support in tuberculosis and may persist for least 6 months after the start of treatment. Whatever the metabolic mechanisms responsible for change in body composition in HIV/AIDS, they may be different from those

present in chronic food insufficiency or loss of weight due to cancer. Loss of protein mass is markedly accelerated during opportunistic infections. It is not, however, clear why some patients experience a starvation-like metabolic response whereas others, especially those with Pneumocystis carinii infection, for example, may experience a hypermetabolic state. Endocrine changes have been noted in chronic dietary deficiency and certain infections but their contribution to metabolism and changes in body composition seem particularly striking in HIV/AIDS. Gonadal function is altered in HIV infection and hypotestosteronaemia may result in substantial loss of muscle mass. Screening for hypogonadism as part of the clinical assessment of HIV-infected subjects provides the potential for endocrine treatment as a means of enhancing lean body mass; this is discussed below. Loss of body protein during HIV/AIDS is therefore caused by poor diet, malabsorption, endogenous intestinal losses and altered metabolism; all are more striking during opportunistic infection. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

Depletion of protein stores adversely affects many aspects of morbidity and mortality from infectious disease. Early studies of HIV suggested that mortality correlated with loss of lean tissue rather than overall weight loss. More recent studies support these findings.

However, the close association between the immune suppression from HIV, changes in blood levels of nutrients as a results of inflammation, opportunistic infection and loss of lean body mass makes it difficult to determine how much the morbidity and mortality from an immunologically crippling disease are is further contributed to by loss of body protein. The absence of carefully performed trials of nutritional supplementation makes it difficult to be absolutely certain as to how much nutrition interventions will improve the outcome of HIV/AIDS. However it possible to extrapolate from the many studies of the effect of nutritional interventions in other diseases; there are many examples of benefits in terms of progression, severity and survival among children with malnutrition and other diseases. There are many interventions possible to overturn the detrimental effect of severe malnutrition in other diseases in children and adults. It seems reasonable to assume that nutritional interventions in HIV/AIDS will enhance defence against infection, promote recovery and improve quality of life and survival despite the lack of properly conducted trials. In a cohort of relatively healthy HIV-positive adults, benefits of intervention in terms of

well being and physical functioning score were rather small but there are many anecdotal reports of considerable weight gain as patients become effectively treated with ARVs. Indeed the absence of food seriously impairs the ability to respond to ARVs effectively. Studies of nutritional therapy in TB show improved rates of growth and muscle power if they are given food rather than advice alone. Such benefits may be of interest to a sedentary worker.\They are likely to be saving for a manual worker and his/her family.

Several studies show the benefits of graded exercise schedules on body composition and wellbeing. Those with severe HIV/AIDS associated wasting have profound fatigue and are unlikely to be able to maintain high levels of physical activity. However physical activity needs to be considered more positively as a means of rebuilding muscle protein stores. Many of the quality-of-life assessment instruments are specific to the cultures for which they were developed. Within the same country some who have lost weight will not feel able to work at their office or farm whereas others with similar body composition will be able to work. Globally, HIV-associated protein depletion is likely to have a major effect on work output and thus on the ability of an individual to generate income or produce food in economies without a well-developed welfare system. This will adversely affect the future nutritional state in a self-perpetuating spiral. Levels of lean body mass or body mass index at which function - whether physical activity, immune tolerance, recovery from illness or other measure - declines has not yet been determined for patients with HIV/AIDS. In the meantime there is enough evidence that overcoming even moderate malnutrition will have considerable benefits for health, development and survival.

Loss of body protein plays a key role in reducing immune system, delaying tissue repair and slowing recovery after opportunistic infection. Recovering it requires a combination of improved infection control, increased food availability including items which are palatable for those with anorexia) and compassionate care and support. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

Plasma levels of most acute phase proteins are altered in HIV, even in asymptomatic cases. The role of these proteins in contributing to host immunity and carrying micronutrients in blood to tissues is increasingly recognized. Levels of acute phase proteins in the blood are controlled by changes in production in the liver and breakdown in the liver and other tissues together with alterations in the various pools

of these proteins in the body. Measurement of some of these processes provides an understanding of how their levels in blood and tissues are controlled. The changes in acute phase proteins appear to be more related to severity of the infection and metabolic stress than to nutritional status or dietary intake. It is not yet clear how the changes in blood levels come about. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

On the other hand, protein metabolism in humans can only be measured in several ways. Whole-body protein turnover, an index of the rate at which amino acids are utilized from blood for protein synthesis and released from protein breakdown, is usually measured by using stable isotopes. A greater understanding of the flow of nutrients in HIV/AIDS will lead to more effective formulations of for treating people with HIV/AIDS and malnutrition. For this reason it is helpful to review the results of such studies even if they do not – for reasons of difference in study subjects and methodologies – produce consistent results. Asymptomatic HIV-positive subjects show faster release into the circulation of leucine and glutamine after an oral dose or intravenous dose. This indicates faster rates of turnover of body protein, even without opportunistic infection and explains why some of the blood levels of “inflammatory” and “carrier” proteins change in early infection. Rates of protein turnover are usually increased in HIV/AIDS. These processes require extra energy. They may account for the extra 10% of energy that is required in HIV/AIDS, even in asymptomatic subjects.

There is debate about how well metabolism responds to feeding in HIV/AIDS. Some studies indicate normal response, even among those not receiving ARVs, whereas other studies indicate reduced anabolism in HIV/AIDS. These differences may be due to differences in degree of disease, nutritional status, recent dietary intake or even type of ARV. Several mechanisms have been suggested. Skeletal muscle and visceral protein are the major components of body protein. Stable isotopes have been used to study the impact of HIV/AIDS on muscle protein as opposed to visceral protein.

HIV/AIDS `affects protein metabolism in different ways in different tissues. During an acute phase response there is a particular propensity to lose muscle protein. Studies on visceral protein during infection are few. Overall, protein loss occurs because of an imbalance between building up (anabolism) and breaking down (catabolism). There are many factors which influence whether an anabolic process can increase or a catabolic process can decrease in the presence of infection. Defining and

evaluating a series of formulations which are effective at improving muscle mass by means of reducing catabolism or increasing catabolism remains a research priority. In the meantime the overall evidence suggests that protein intake should be increased by 10% to match the increased intake of energy that is needed in HIV infected people. This should be continued to maintain body nutrient stores during the chronic asymptomatic phase of HIV. When immunity fails and an opportunistic infection occurs, encouragement should be given to the patient to keep going with the extra 10%. It is unlikely that they will be able to eat any more than this if they are feeling unwell. Indeed special, appetizing formulations of food will be necessary, especially for children, to achieve their maintenance dietary intake. Once the opportunistic clinical infection has cleared, additional amounts of energy and protein up to 30 – 50% over the customary intake should be encouraged to achieve nutritional recovery. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

Muscle protein wasting occurs in human immunodeficiency virus (HIV)-infected individuals and is the initial indication of acquired immunodeficiency syndrome (AIDS).

The metabolic mechanisms of muscle protein wasting in HIV-positive patients are not completely understood. There are two key forces are at work – negative energy balance and the cellular effect of the virus and its opportunistic infections. It has been suggested that patients with AIDS who have increased whole-body protein synthesis cannot increase rates of muscle turnover to the same degree. This implies that protein turnover and synthesis in the viscera are markedly increased, and considerable evidence for this exists. Several studies show greatly increased metabolic activity in the liver. Studies using 3 methyl-histidine have given considerable insight into factors controlling muscle breakdown. The marked changes in plasma levels and turnover of acute phase proteins are striking. The rates of whole-body protein turnover in patients with HIV infection are generally increased. Considering the severity of the clinical sepsis, it is surprising that the rates are not even higher. Deficiencies of threonine and methionine were reported as rate limiting for whole-body protein synthesis in AIDS patients.

Overall, most studies show that abnormal rates of whole-body protein turnover occur in HIV/AIDS and that they are considerably affected by energy balance, which is vital for maintaining normal protein metabolism. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

1.4.3. Fat Requirements

The most important functional components of dietary lipids (triglycerides, cholesterol esters and phospholipids) are fundamental to normal growth and development of infants. Fatty acids are classified according to their chain length and their degree of saturation. Each class of fatty acid is involved in specific metabolic reactions: short-chain fatty acids act as local growth factors in the colon; medium- and saturated long-chain fatty acids are a good source of energy; poly-saturated long-chain fatty acids are involved in metabolic regulation; and very long-chain fatty acids are important structural components of membranes. The central nervous system development depends on the amount and the quality of the lipid consumption in the last months of prenatal and the first months of postnatal life. Fats in breast milk provide half the infant's calorific needs and maternal dietary habits can influence the lipid composition of milk. Any abnormality or a dysfunction in lipid metabolism causes serious problems in the body. (M Giovannini, 1991)

a) Lipid metabolism

Abnormalities of lipid metabolism are seen in HIV-positive patients, especially those receiving ART/HAART. Fat oxidation increases in HIV-positive patients but carbohydrate oxidation is suppressed in AIDS, suggesting that more fat than carbohydrate is used as fuel source. Lipoatrophy in HIV-positive patients with lipodystrophy syndrome is associated with accelerated lipolysis, which leads to futile cycling. In addition, lipodystrophy contributes to insulin resistance in HIV-positive patients, increasing the risk of diabetes mellitus. It is not known whether patients who are undernourished at the time of HIV diagnosis are more or less susceptible to lipodystrophy development. Arguably, those on low-fat diets may have less endogenous fat production and therefore less low-density lipoprotein cholesterol. Some studies showed an increase in the prevalence of lipodystrophy among those

with low body mass index and inferred that malnutrition may actually increase the susceptibility to side effects from antiretroviral (ARV) therapy. A greater understanding of what body tissues change in response to the disease and to the treatment will be necessary for developing better nutrition and ARV regimens for patients with HIV/AIDS. Marked changes in plasma lipids, attributable to HAART, require novel dietary and pharmacologic interventions. (Grobler L, 2013)

b) Endocrine factors

Testosterone enhances muscle strength, oxandrolone enhances lean body mass, recombinant growth hormone reduces visceral fat and buffalo humps but has a lot of side effects, oxymetholone improves muscle mass and metformin and rosiglitazone change fat distribution. Rather remarkably, the molecular basis for these actions, which are becoming more prevalent in patients taking ARVs for long periods, is almost completely unknown. Subcutaneous adipose tissue has been studied in HIV-positive subjects and glycerol release was noted to be higher in HIV-positive than -negative patients. Tumor necrosis factor release from subcutaneous adipose tissue and serum soluble tumor necrosis factor receptor 2 concentrations were also significantly higher in HIV-positive individuals with lipodystrophy. The absolute production of acylation-stimulating protein and the percentage conversion of the complementation protein to acylation-stimulating protein are significantly lower in HIV-positive subjects with lipodystrophy. Plasma adiponectin and leptin levels are altered in HIV but both elevated and depressed levels occur in lipodystrophy; adiponectin deficiency may play a role in the insulin resistance associated with HIV lipodystrophy. Endocrine treatment has a potential role in the management of the lipodystrophy syndrome and may stimulate a metabolic response in HIV infected adults and children. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

1.5 Nutritional Stages of HIV/AIDS according to WHO

The nutritional status of patients with HIV/AIDS depends on the availability of food and appropriate nutrient supplements, the period of illness and access to treatment with ARVs and prophylactic and therapeutic antibiotics and the presence of people to

encourage them to feed and support them as they overcome the illness. A provisional scheme is shown here by WHO, Department of Nutrition for Health and Development, 2005:

Stage A – Where ARVs are available, additional food is available for the patient to respond to improved appetite once they go on ARVs, there is good quality dietary support to advise on best dietary ways of optimizing effect of ARVs, there are special preparations to eat during illness from opportunistic infections and patient care and support is available – weight gain can be rapid, but may be more fat than protein.

Stage B – Where ARVs are available, additional foods are available for the patient to respond to improved appetite once they go on to ARVs, there are special preparations to eat during illness, but there are metabolic complications requiring dietary/ clinical advice – weight gain can be rapid but lipid and metabolic profiles are hazardous in the short and long term.

Stage C - Where ARVs are available but additional food is not available, even though patient care and support is. Nutritional recovery is frustratingly slow and opportunistic infections are more common and life threatening. Side effects of drugs may prevent compliance.

Stage D - Where ARVs are unavailable but additional food and patient care is. Nutritional support can achieve nutritional recovery and is likely to delay disease progression, decrease morbidity and improve survival. Nutritional recovery is slow depending on how much catch up/recovery can be achieved between infections.

Stage E - Where illness is severe, ARVs are unavailable, additional food is not available but patient care and support is available. Nutritional recovery is extremely difficult but possible.

Most studies have been among patients in Stage A or B in industrialized countries. Some patients benefit from dietary counseling and supplementation; others require tube feeding and even gastrostomy. Patients with HIV/AIDS and weight loss are metabolically analogous to patients with cystic fibrosis. Both groups have high levels of circulating cytokines and increased RMR during infective episodes. Nutritional support is largely ineffective until the infections are treated. However, there are window of opportunity between acute infective episodes. Supplemental energy and protein are largely effective in restoring body weight but their effect on achieving restoration of body protein as opposed to fat is not clear. These factors have been taken into account in the production off new equations for calculating resting energy

expenditure in patients with HIV/AIDS. It is hoped that these may be used to calculate a more tailored energy requirement for an individual. Anabolic hormones such as human growth hormone and androgens have been advocated but no study has yet compared the effect of anabolic hormones with dietary supplements. Studies on growth hormone supplements have been limited to N. America. Few studies have examined the effect on body weight or composition of particular nutritional supplements (e.g. special preparations formulated with particular focus on certain amino acids) compared with conventional clinical supplements such as Sip Feeds. Despite a lot of problems in relation to diseases severity, availability of ARVs and the physical and socio-economic environment there are many things that can be done for patients with HIV/AIDS. At the every least, increasing their dietary and protein intakes in the period after recovery from opportunistic infection is likely to be beneficial in the short and long term. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

1.6 Nutrition Interventions

The main nutrition interventions are counseling on specific behaviors, prescribed/targeted nutrition supplements, and linkages with food-based interventions and programs.

Three different types of nutrition supplements are considered: food rations to manage mild weight loss and nutrition-related side effects of ARV therapy and to address nutritional needs in food insecure areas; micronutrient supplements for specific HIV-positive risk groups; and therapeutic foods for rehabilitation of moderate and severe malnutrition in HIV-positive adults and children. The basic actions are shown in the table 9.

Table 9: Summary of Nutrition Interventions according to HIV Disease Progression (USAID, 2004)

Intervention	HIV+ Asymptomatic	HIV+ Symptomatic	AIDS	Families affected by an HIV-related Death
Counseling/care	Nutrition education and counseling for positive living	Nutrition management of HIV-related opportunistic infections (OI), symptoms, and medications	Nutrition management of ARV therapy Nutrition management in home-, clinic- and community-based, palliative care	Counseling on special food and nutritional needs of orphans, vulnerable infants, and young children
Prescribed/ targeted nutrition supplementation	For high-risk groups only (e.g., pregnant and lactating HIV+ women, HIV exposed non-breastfed children)	For high-risk groups For persons who are losing weight or do not respond to medications Therapeutic feeding for moderately	Therapeutic feeding for moderately and severely malnourished HIV+ adults and children	For high-risk groups (e.g., HIV-exposed non-breastfed children < 2 years or HIV-exposed children with growth faltering)

		and severely malnourished HIV+ adults and children		
Other food interventions	To prevent nutritional deterioration for HIV-affected families living in highly food insecure communities	To improve adherence/ participation in OI treatment programs	To improve adherence/ participation in ARV and OI treatment programs To use in home-, clinic-, and community-based care programs	To protect the health of orphans and vulnerable children and for surviving family members when livelihoods are compromised because of HIV related sickness or death

1.6.1 Protein/Energy supplementation

Achieving increased protein intake results in an increased body cell mass in HIV-positive men. Nutrition interventions combined with dietary counseling alter reduce loss of body protein by reducing whole-body protein breakdown. An RCT compared nutritional counseling alone with supplements given for 6 weeks. There was

increased energy intake but no discernible effect on body composition or quality of life. A longer 6-month study including supplements with arginine and omega-3 fatty acids failed to show significant benefit in terms of body composition compared with results observed in a group of control patients receiving dietary advice alone.

Nevertheless, some studies have shown benefits from supplementation. Berneis et al. gave supplements to 15 subjects in a small randomized trial lasting 3 months; supplements provided about 17% of energy from protein and resulted in an increase in protein intake of about 20 g/day. The subjects gained lean body mass (measured by bio impedance analysis) and had slower rates of whole body protein catabolism measured by leucine kinetics. One study sought to demonstrate rate limiting amino acids for protein synthesis by looking for a lack of rise in plasma level when amino acids were administered as part of a complete amino acid–glucose mixture for 2.5 hours; the authors suggested that threonine and methionine may be rate limiting for whole-body protein synthesis in AIDS patients. A comparison of formula supplemented with α-linolenic acid, arginine and RNA with a standard formula in a double-blind crossover study found greater weight gain with the supplemented formula. This was associated with modulation of pro inflammatory cytokines, including tumor necrosis factor, by the special formula. (WHO, 2005)

Where dietary intake is already satisfactory, supplements are unlikely to be beneficial. Where the patients are relatively free from opportunistic infection, supplements can restore lean body mass.

No evidence exists for advocating a particular formula; such data are needed. Different types of dietary protein preparation have been advised but there is insufficient evidence to recommend one regime over another. (Jean W-C. Hsu, Paul B. Pencharz, Derek Macallan and Andrew Tomkins, 2005)

<u>As “Ready to use therapeutic foods”; RTUF and HEBI:</u>

There is a useful study from Vietnam. Vietnam’s HIV prevalence is low, estimated at 0.45 percent among people 15–49 years old in 2011 (Ministry of Health 2011), although this figure means a significant number of HIV-positive individuals in a population of almost 89 million (General Statistics Office of Vietnam 2012).

Ready-to-use therapeutic food (RUTF) has been found to be a highly effective and relatively inexpensive intervention to treat severe acute malnutrition (SAM) among

people with or without HIV. The most commonly used RUTF for this purpose has been the peanut-based Plumpy'Nut produced by Nutriset. But there were communication and infrastructure problems in the communities exposed to Plumpy'Nut that were unrelated to taste and acceptability. Because of the negative findings of this investigation and the high cost of importing RUTF in Vietnam, the National Institute of Nutrition (NIN), the Institut de recherche pour le développement (IRD), and UNICEF collaborated in 2009 to formulate a rice/soy/mung bean-based RUTF that could be produced locally. The product of this effort is called High-Energy Bar for Integrated Management of Acute Malnutrition (HEBI). In 2010 a small acceptability study conducted among moderately malnourished HIV-negative preschool-age children in Vietnam concluded that HEBI was sufficiently acceptable to be considered a potential intervention for this population.

Table 10: Comparison of UNICEF RUTF requirements and HEBI specifications

Component	**UNICEF product specifications for RUTF**	**HEBI specifications**
Energy	520–550 kcal/100 g	547 kcal/100 g
Weight	92 g/sachet	92 g/sachet
Protein	> 50% from milk 10%–12% kcal	52.4% from milk 12% kcal
Lipids	45%–60% kcal n-6 fatty acids: 3%–10% kcal n-3 fatty acids: 0.3–2.5% kcal	58.7% kcal n-6 fatty acids: 8.8% n-3 fatty acids: 2.2%
Moisture content	< 2.5%	< 2.4%
Heavy metals	None	Lead: None detected Cadmium: None detected Arsenic: 0.02 mg/kg Mercury: 0.01 mg/kg

Pesticides	No hazardous levels	None detected
Microorganism count	< 10,000 CFU/g	450 CFU/g

Source: UNICEF/Vietnam and NIN. 2011.

Ready-to-use therapeutic foods (RUTFs) are edible, homogenized, energy-dense, lipid-based foods with added vitamins and minerals. It does not need to be prepared before consumption, making it practical where cooking fuel and sanitary cooking facilities are limited. Because RUTF is not water based, it does not risk significant bacterial growth and the foods can be stored and used safely at home and used in community-based management of acute malnutrition. RUTF has been shown to improve the nutritional status of children living with HIV and is easy to eat for adults with mouth sores or other HIV-related symptoms. (FANTA, 2013)

1.6.2. Micronutrient Supplementation

The role of micronutrients in immune function and infectious disease is well established. However, the specific role of individual and multiple micronutrients in the prevention care and treatment of HIV infection and related conditions merits further attention. Several studies on micronutrients and HIV are under way, and new findings should be available soon.

Observational studies indicate that low blood levels and decreased dietary intakes of some micronutrients are associated with faster HIV disease progression and mortality, and increased risk of HIV transmission. However, these studies' methodological limitations preclude definitive conclusions about the relationship between micronutrient intake and blood levels, and HIV infection.

Some studies show that there is evidence that supplements of, for example, B-complex vitamins, and vitamins C and E, can improve immune status, prevent childhood diarrhoea and enhance pregnancy outcomes, including better maternal prenatal weight gain and a reduction of fetal death, preterm birth and low birth weight. The effect of these micronutrients on HIV disease progression and mortality is under study. Micronutrients that have produced positive health outcomes in HIV

uninfected populations include zinc supplementation for reducing diarrhea and pneumonia morbidity in children. The safety and effectiveness of zinc supplements in HIV-infected adults and children are now being studied. (WHO, 2003)

Research has been far more extensive on the role of vitamins and trace elements in HIV infection. Observational studies show associations between low serum concentrations of vitamin A, vitamin E, vitamin B12, and zinc and disease progression and/or negative health outcomes. A large randomized controlled trial in Tanzania showed that multiple micronutrient supplementation (vitamins A, C, E, and several B vitamins) increased CD4+ and CD8+ cell count, but vitamin A alone had no effect. In a different study, high-dose vitamin A supplementation of pregnant women appeared to increase the risk of mother-to-child transmission in Tanzania but the same effect was not observed in a study carried out in South Africa. A study in Zambia failed to show a positive effect of supplementation with multiple micronutrients (vitamins A, C, and E, selenium, and zinc) on persistent diarrhea in HIV-positive adults but HIV-positive TB patients in Tanzania had a 70 percent reduction in mortality when they were given a mix of micronutrients including zinc and, in a separate study, provision of daily multivitamin supplements to HIV-positive women in Tanzania was shown to reduce the risk of death by 50 percent. Because some micronutrients (especially vitamin A and iron) in higher doses have been associated with negative outcomes, it would seem prudent to use lower, more physiological doses (minimum doses needed to produce a physiological effect in the body) for interventions targeted to PLHIV. (FANTA, 2013)

There are other problems which causes of deficiencies. Anemia is a common problem for PLHIV and contributes to fatigue and malaise as well as increasing the risk of HIV disease progression. There are a number of different causes of anemia in PLHIV including:

Deficiency in iron, B12 or folate from inadequate intake or malabsorption

- Chronic illnesses such as TB and malaria
- HIV medications, particularly Zidovudine
- Increased iron needs ex: pregnancy
- HIV infection per se
- Blood loss. (Houtzager, 2009)

The best way to prevent anemia is by eating a wide variety of nutritious food. Iron absorption is influenced by the body's stores of iron. It is not just the amount of iron in the diet is important, but the amount that the body can absorb. Iron supplements may be beneficial in deficiency states but there are reports of deleterious effects in ongoing infections including malaria. Current guidelines for iron supplementation are unclear and a recent Cochrane review concluded that "the current clinical practice of iron supplementation in HIV-infected children is based on weak evidence comprising observational studies and expert opinions" and that high-quality RCTs of iron supplementation are urgently required, especially in areas with significant overlap of high prevalence of HIV, iron deficiency anemia, and malaria.

Some studies suggest a benefit in using micronutrient supplementation to slow HIV disease progression. A study in Tanzania found that women who received high dose multivitamin supplementation were less likely to have progression to advanced stages of HIV infection. These findings were supported by a study of HIV positive males and females with advanced symptoms in Thailand which showed decreased rates of death in adults who received high dose micronutrient supplementation (Houtzager, 2009).

2. MATERIAL and METHOD

a. Design and area of the study

A total of 49 people living with HIV (45 male, 4 female) completed this study which was approved by Ethics committees in Turkey, Yeditepe University Hospital Ethics Committees. A HIV counseling community (Positive Living Association, 2005), carried out the survey. The survey prepared by the researcher and the advisor.

The design of the present study was cross-sectional. The self-administered and the advisor structured questionnaire survey was conducted between September 2014 and February 2015 in a counselling community (Positive Living Association), which is a non-governmental organization, in İstanbul, Turkey. The surveys are carried out by the counselling office because of the privacy statement. Only the counselor interviewed with the HIV positive volunteer. Positive Living Association (PLA) has been working according to the objectives that have been determined by process of strategic planning since 2005. PLA has so many important experiences and it has developed quickly. Positive Living Association is an association that was established by people living with HIV/AIDS, their relatives, volunteers, and experts on related branches.

b. Study population and sampling procedures

The sample size is determined by the power analysis method. The present study is a cross- sectional study. In this study, the 49 volunteer joined the survey and the average age of this population was 33.2 years old. The gender distribution of the population is 91.84% male and 8.16% female. The volunteers are surely not under age 18. And it is based on being volunteer.

The sampling unit was the Positive Living Association, İstanbul. The reasons why the PLA was chosen for the study are, they have enough capacity to find volunteer for the surveys and both newly and lately diagnosed HIV positive people are canalized to this association.

c. Data collection

A detailed questionnaire was used for data collection. The survey contains 4 part;

- First part is the basic information (age, gender, height, weight) about the volunteer but not the private information (name, surname etc.),
- Second part contains the medical information like the routine tests, the drugs which is used, the drug resistance tests,
- Third part is general health information like the weight losing, digestive system problems, supplements which are used, and the community which the meals are eaten with.
- The fourth part contains the food record which is collected with 24-hour recall data survey.

The questionnaire was originally written in Turkish and later translated into English. Translation were done by the researcher and the advisor.

At the end of each month, the surveys are taken by the researcher from the collaboration committee. Survey numbers are added to the each survey. These meetings were used as an opportunity for controlling the quality of information through checking the questionnaires for completeness.

A systematic literature review was carried out. Studies were identified through 3 methods: (1) computer searches of MEDLINE, PubMed, EBSCOhost databases from 1985 (the year that HIV antibody testing was approved for public use) through 2015, using combinations of the key words; HIV, AIDS, NUTRITION counseling, and ART (2) manual searches of the journals AIDS, AIDS Care, AIDS Education and Prevention, Cambridge Journals, American Journal of Public Health, Health Psychology, Journal of the American Medical Association, and Sexually Transmitted Diseases (current) and (3) inspection of the reference lists of all identified articles. Not only about the nutrition in HIV, but also all periods of HIV was researched.

d. Ethical considerations

Prior to the study, ethical approval was sought and obtained from the Yeditepe University Hospital Ethics Committees in Turkey, The research permit and approval

to conduct the study were sought and obtained from Yeditepe University Hospital Ethics Committees.

The positive living association was briefed about the study before they meet the volunteers.

Informed consent was sought and obtained from participants before they filled in questionnaires by the PLV workers. Specifically, participants were informed about the objectives of the study and were informed that their participation was purely voluntary and they were free to decline or withdraw at any time in the course of the study. It was transparently clarified that the information provided whether orally or in writing was for research purposes and would therefore be strictly anonymous and dealt with confidentially.

e. Data analysis and statistical procedures

The data were analyzed quantitatively using SPSS for windows (Version 18.0)

Analyses varied according to the papers. In general, descriptive and association statistics were employed.

The medical and general information (the routine tests, the drugs which is used, the drug resistance tests, weight losing, digestive system problems, supplements which are used, and the community which the meals are eaten with.) were analyzed as frequencies, percentages, mean, and standard deviation. And with the cross tables, connected information were found (BMI and the weight loss or age and meal habits) The p-value ≤0.05 will be considered statistically significant.

This survey contains basic personal HIV information and 24 hour recall survey. Researcher expected that the basic data will show that the food consumption habits. The calculations are done with a food information system which is called BEBIS. With the results of BEBIS, calculation of total energy, macronutrient and micronutrient consumption, food consumption were done. BMI can be compared to healthy people. The system collects the dietary information as described by the survey participant and automatically translates this descriptive information into food codes and quantities for subsequent by a nutrient analyze system.

3. RESULTS and DISCUSSION

In this study, the 49 volunteer joined the survey and the average age of this population was 33.2 years old. The age range of the study has an intensive distribution between 18 and 24. The gender distribution of the population is 45 male (92%) and 4 female (8%) (Figure 5). The average BMI of the population is 23.8kg/cm^2

The average energy consumption in a day is 1373kcal/day, and it supplies the %67 of daily recommended energy intake.

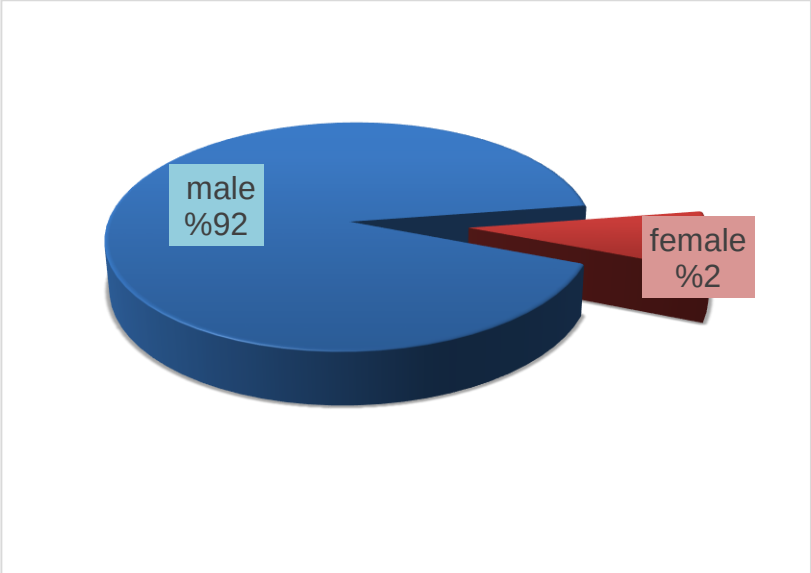

Figure 5: Gender distribution of the study population

According to the Ministry of Health study, which has done in 2013, shows that, the 73% of the HIV positive population in Turkey is male. The dominant majority of the male HIV positive individuals have always been since 1985. (MoH, June 2013).

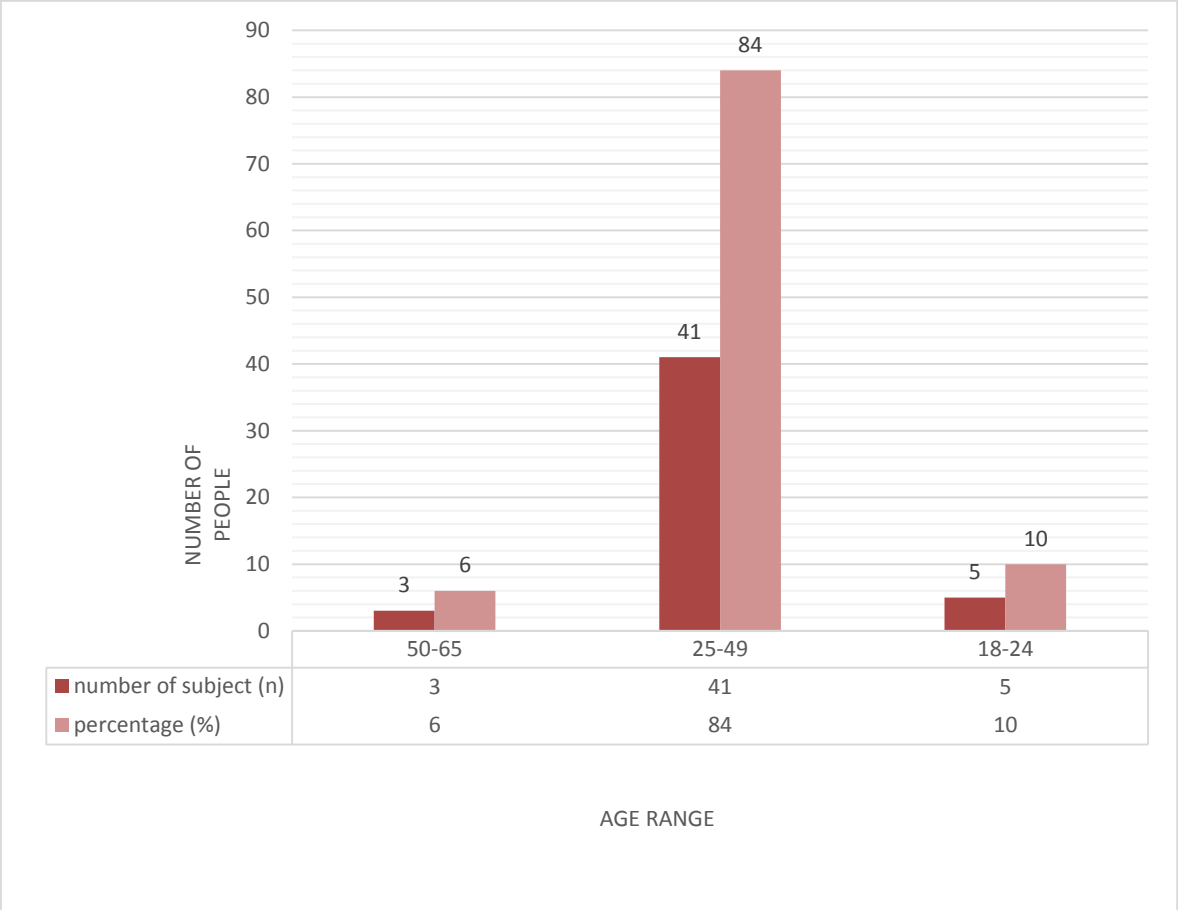

Figure 6: Age distribution of the study population

Women constituted 22.9% of the total cases which were reported in 1985-1996, 37.4% in 1997- 2001, 31.4% in 2002-2006, and 26.3% in 2007-2011 period. When the age distribution of cases was examined, it was observed that the first two ranks were shared by 20-29 and 30-39 age groups, and the proportion of the age groups over 40 years of age was increasing by the time (Erbaydar, 2012)

In this study (figure 6) the age distribution has a high intensity (84%) between 25-49 years old. And 5 people (10%) is between 18-24 age range, 3 people (6%) is between 50-60 age range. For the study, age ranges are determined according to WHO age period definition. If the 25-49 age range divided to 25-35 and 35-45, 45-55 the distribution of number of people according to these age ranges are 28 individuals for 25-35 age range, 10 individual for 35-45 age range range and 6 individuals for 55-65 year range. It is clear that the age range between 25-35 has a major intensity (57%) in the population.

Table 11: Energy consumption compared to the RDI values

% of required energy	number of people	% of total population
≤ 49 %	16	33%
50-99%	23	47%
≥ 100%	10	20%
	n=49	total= %100

*Required energy is calculated as 2000kcal/day

As it seems in table 11, the 16 subject in the study population supplies the ≤ 49% of daily recommended energy need. The 23 subject in the population supplies 50-99% of the daily recommended energy need. Only the 10 subject takes adequate amount of the energy in a day. When the statistical data is analyzed, the subjects whose energy consumption is high than 100% of RDA, some specific food consumption has been saw. Alcohol consumption, high energy bars, high energy drinks, high sugar consumption (with tea or coffee) reduces the percentages of daily energy consumption percentages.

In a cohort study which consisted of 886 patients, of which 28 (3%) were underweight. Of the remaining 858 patients, 448 (52%) were normal weight, 294 (34%) were overweight, and 116 (14%) were obese.

Similar to U.S. studies, their (Messina et. al.) findings suggest that being overweight or obese is more common than being underweight in an urban, outpatient population of PLWH. (Messina, 2014)

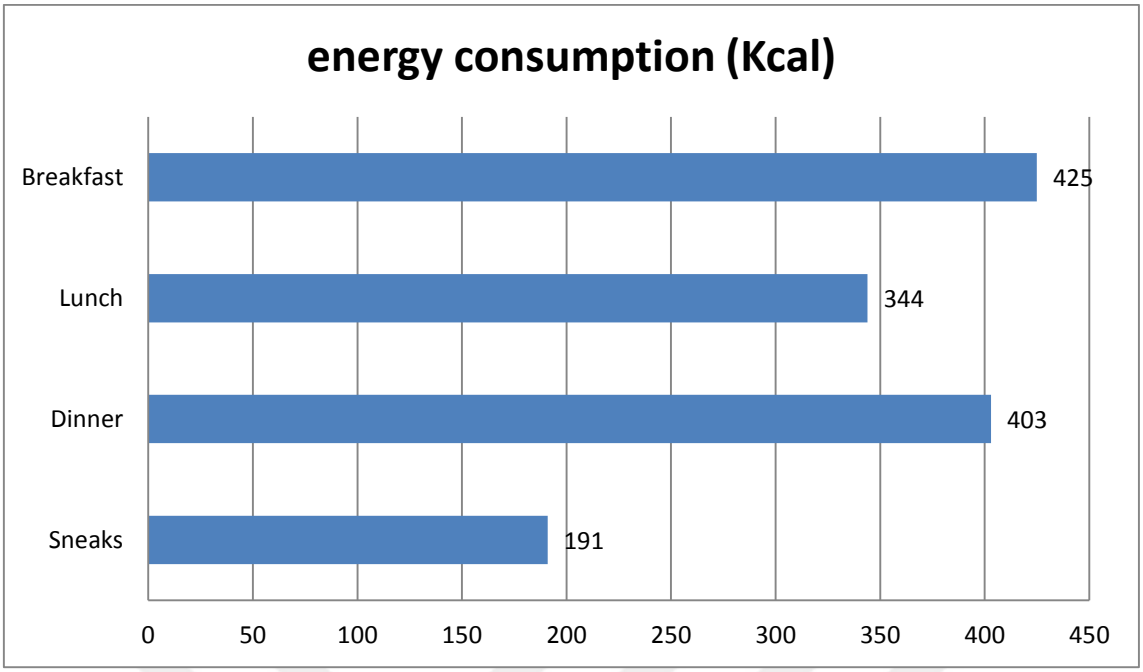

Figure 7: Energy consumption in meals

As it seems in figure 7, the daily energy consumption has a close division into three mean meals. The energy consumption average is 425kcal/day (35%) at breakfast, 344kcal/day (29%) at lunch and 403kcal/day (36%) at dinner.

When the sneak habits are analyzed, it is seen that 30 individuals (62.1%) in the population having sneaks during the day. Only the 5 of them have three sneaks in a day. The 9 of the population have first two sneaks. And 14 HIV positive individuals have only the after dinner snake.

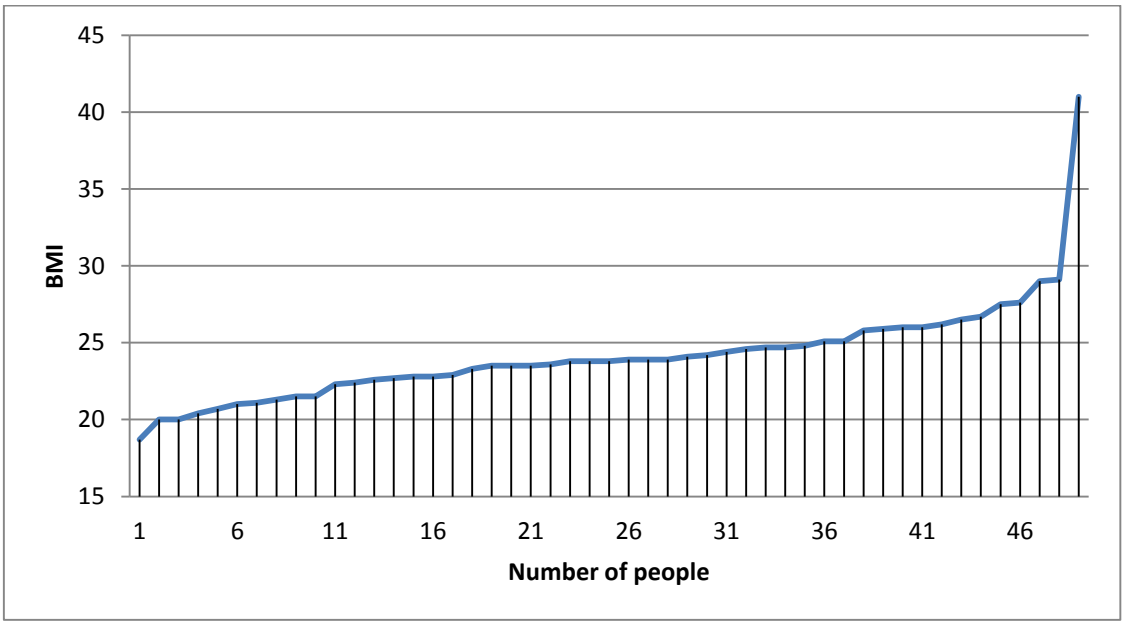

Figure 8: BMI distribution in study

The average BMI value of the study population is 24.1 kg/m$^{2.}$ In this study, as it seen in figure 8, 35 of 49 subjects have normal BMI value, 13 of 49 subjects have overweight BMI value and 1 of 49 subjects has a morbid obese BMI value. There is no subject who has the BMI value less than 18 or 25-30. The average BMI of the population is 24.1 kg/m$^{2.}$ It includes one subject who has 41 for BMI value. This effects the average value but when we calculate the average value without 41, it is also in normal range (23,8 kg/m^2 ± 2,3).

Table 12: The cross table of length of being HIV positive and BMI value

		length of being HIV positive				
		less than 1 year	2-3 years	4-5 years	6-10 years	11-15 years
BMI	NORMAL	6	18	7	2	2
	OVERWEIGHT	4	5	3	1	0
	MORBID OBESE	0	1	0	0	0
Total	n=49	10	24	10	3	2
%		20%	50%	20%	6%	4%

As it seen in Table 12, there are 35 people who have normal BMI value; 10 of them are living with HIV less than 1 year, 29 of them are living with HIV less than 10 years. The 2 of them have the HIV infection more than 10 years.

When the overweighed people are analyzed, it is seen that there is 13 HIV positive individual in the population and all of them is living with HIV less than 10 years. There is only 1 person in the population who has a BMI value more than 40 kg/m^2. And that person has the HIV infection about 2-3 years.

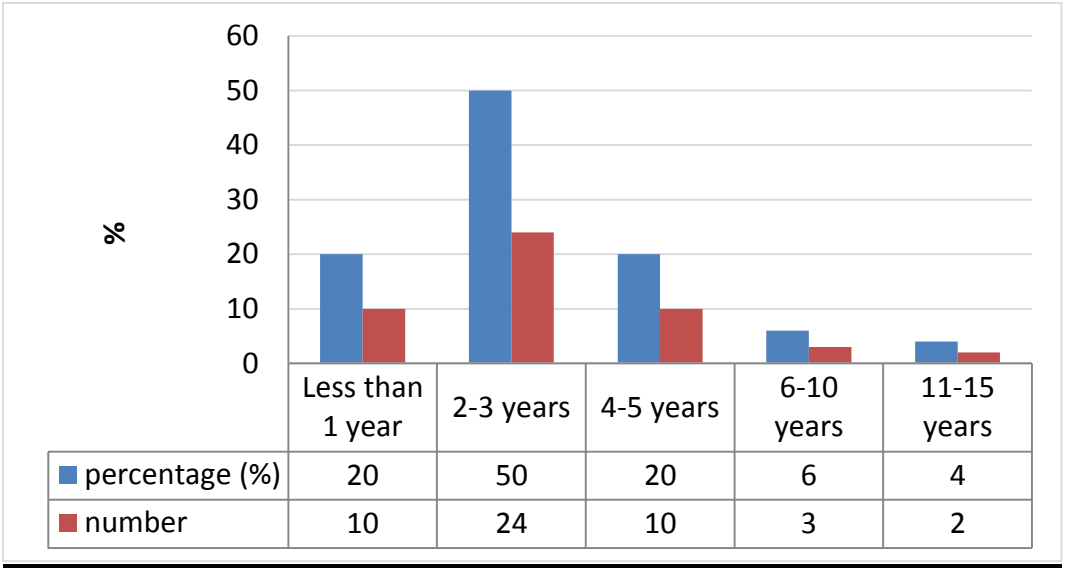

Figure 9a: The distribution of the number of people according to the length of being HIV positive in the study

In figure 9a, the number of people in the survey and the period length of being HIV positive information are matched. The great majority of the study population has Human Immunodeficiency virus for 2-3 years. In the study population, the two groups, which have the virus less than 1 year and 4-5 year, have the same percentage.

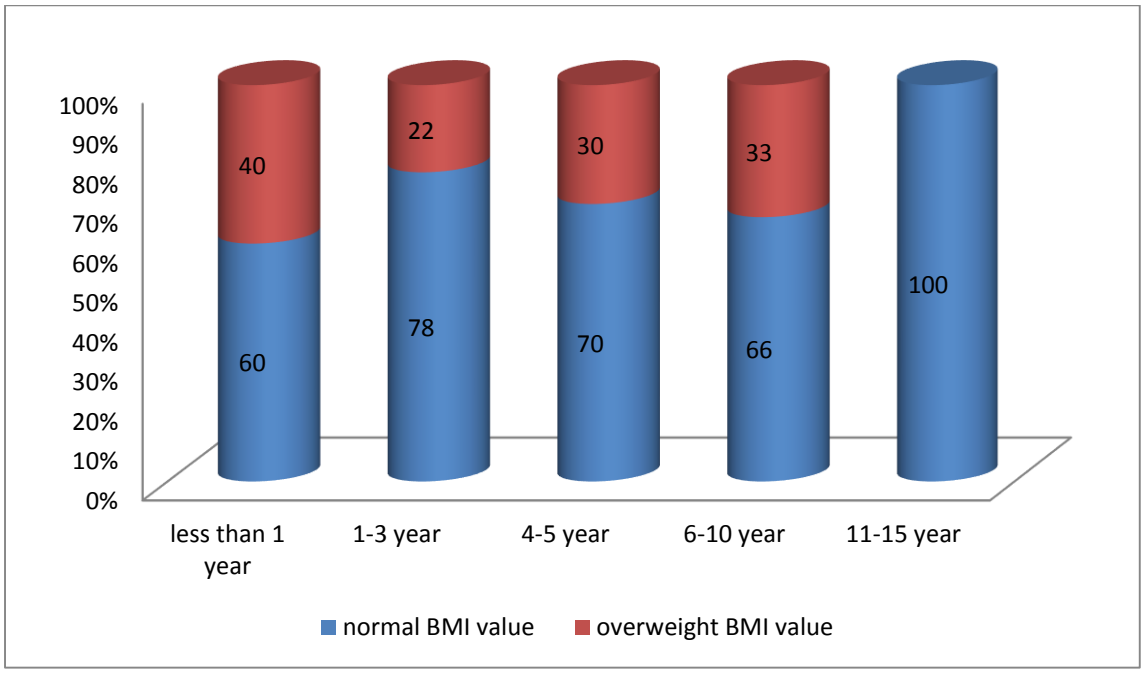

Figure 9b: HIV infection period and BMI values

In figure 9b it is seen that, who has HIV infection less than 1 year, has the biggest overweight percentage (40%) in the study population. Despite of this, the 26% of the study population (n=13), who lost weight in 3 months, 30% of them are living with HIV less than 1 year.

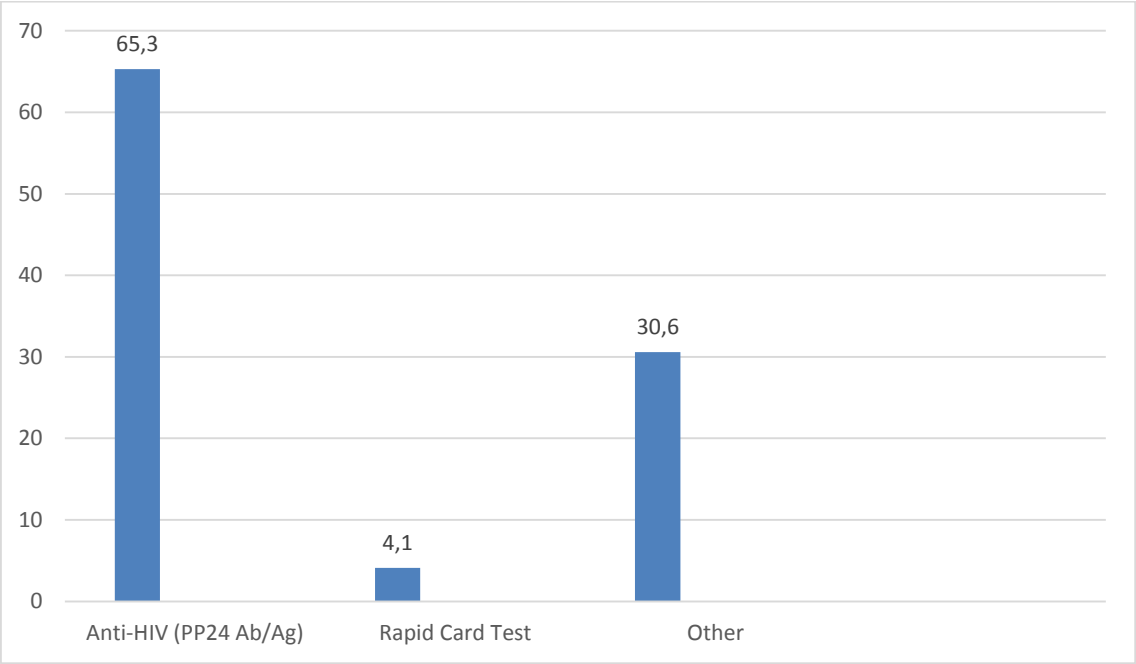

Figure 10: The percentage of people and the diagnose tests

HIV Elisa testing is the first screening test commonly performed for HIV diagnosis because it has a high sensitivity and specificity. Rapid card test are suitable, but its performance is poor by Elisa test for HIV diagnosis. In our study, 4,1 % of participants receiving the first diagnosis with rapid card tests, 65,3 % have been diagnosed with both test (Figure 10). In a study in India, reported highlights that ELISA was a good screening assay for HIV infection. The performance of rapid card test in comparison to ELISA was suboptimal and rapid card test based serial testing algorithm could not parallel the testing accuracy of an ELISA based approach. While false negatives by RDTs increase the proportion of HIV reactive individuals receiving negative reports, false positives by rapid card test are a matter of ethical concern. The diagnostic limitations of rapid card tests can be overcome by possible inclusion of ELISA as a second screening assay, employing rapid card test additionally

detecting p24 antigen as screening assays, and confirmation of reactive samples by western blot to reduce false negative and false positive results, respectively (Mehra, 2014)

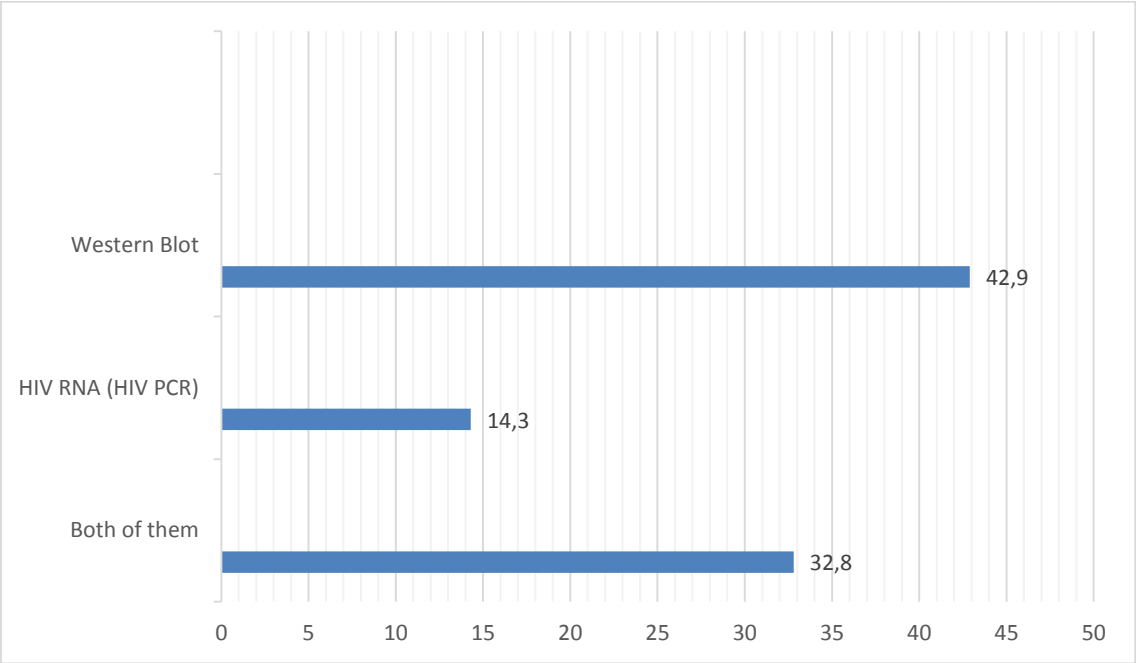

Figure 11: The percentage of people and which test did they use

Western blot is an antibody detection test like Elisa. Elisa is the first choose and western blot is the confirmation test for HIV diagnosis. The Western blot assay is a method in which individual proteins of an HIV-1 lysate are separated according to size by polyacrylamide gel electrophoresis. The viral proteins are then transferred onto nitrocellulose paper and reacted with the patient's serum. Any HIV antibody from the patient's serum is detected by an antihuman immunoglobulin G (IgG) antibody conjugated with an enzyme that in the presence of substrate will produce a colored band. Positive and negative control serum specimens are run simultaneously to allow identification of viral proteins. Antibodies to the HIV-1 major group-specific antigen (GAG) protein p24, and its precursor p55, are the earliest detected after infection by Western blot and tend to decrease or become undetectable with onset or progression of clinical symptom (CDC, 1989)

HIV PCR testing finds HIV virus in white blood cells infected with the virus. PCR testing is not done as frequently as antibody testing, because it requires technical

skill and expensive equipment. In cases where antibody testing may be insufficient to determine whether a patient is infected, it is necessary to perform DNA PCR, a nucleic acid amplification method that allows for the detection of viral DNA integrated into the host cell's genomic DNA (Fearon, 2005)

In our study, 14, 3% of the population have PRC test. 42, 9% of the population has the Western Blot test and 32,8% has the both of them.

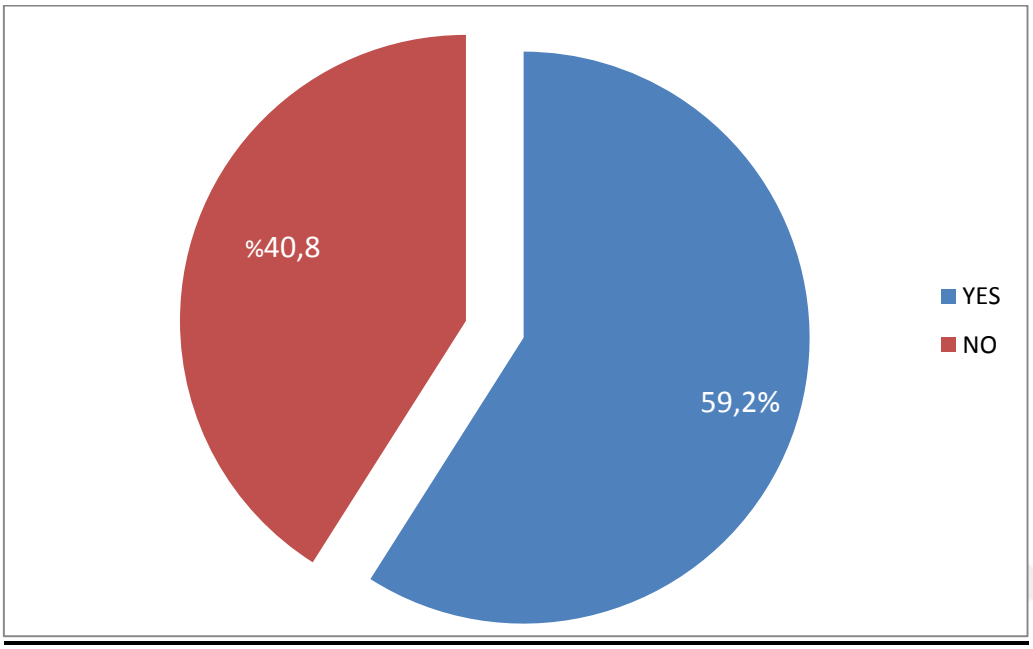

Figure 12: The belief about having enough counselling about HIV

Totally, 59.2% of this population thinks that they have enough counseling about being HIV positive. The more than half of the study population thinks get enough counseling. But we know that there is not enough committee or counseling center in İstanbul or in Turkey. Government support is certainly important for these centers. This study has done in a counseling center that may be the reason why people answer the question in a positive way.

Nutritional counseling should provide guidance for patients to maintain a diet that provides the RDAs or dietary references intake of nutrients. The intake and dietary composition should be adjusted according to the degree of gastrointestinal dysfunction and insulin resistance and may include a low fat, lactose free, low fiber, caffeine free diet.

WHO has issued guidance on HIV testing and counseling (HTC) soon after first HIV tests were developed in 1985. Since that time, WHO has issued guidance on all their forms of HIV testing.

WHO has defined five key components—the “5 Cs”—that must be respected and adhered to by all HTC services. These components are:

- Consent
- Confidentiality
- Counseling
- Correct test results
- Connection/linkage to prevention, care and treatment.(WHO,2015)

There should be pre-test and post-test counseling. Before and after counseling HIV test is important. Because it provides critical information about HIV and testing process. While counseling services may not be available in all health care settings, many testing sites do offer these services. If HIV positive individuals would like access to pre-test and post-test counseling, they be sure to inquire about the availability of these services at their chosen test site. If they do not have them readily available, the staff may be able to direct HIV positive individuals to alternate service providers who do.

Pre-test counseling sessions generally include the following:

- Information about the HIV test—what it tests for, what it might not tell, and how long it will take them to get their results. Explanation the benefits of testing to the individual
- Information about how HIV is transmitted and how people can protect themselves from infection
- Information about the confidentiality of the test results
- A clear, easy-to-understand explanation and details of what the test results mean

Once the results are available, people will usually be given the results in private and in person. Post-test counseling generally includes:

- Clear communication about what the test result means
- HIV prevention counseling, if the results are negative

- A confirmatory test, called a Western blot test, if the results are positive. The results of that test should be available within 2 weeks (aids.gov.tr.) (WHO, 2015)

The World Health Organization also say that the counseling should be face to face especially for likely to have an HIV-positive result, with mental illness or at risk of suicide, for whom has a language problem, under 16 years old, who may be highly anxious or vulnerable and in hospital patients.

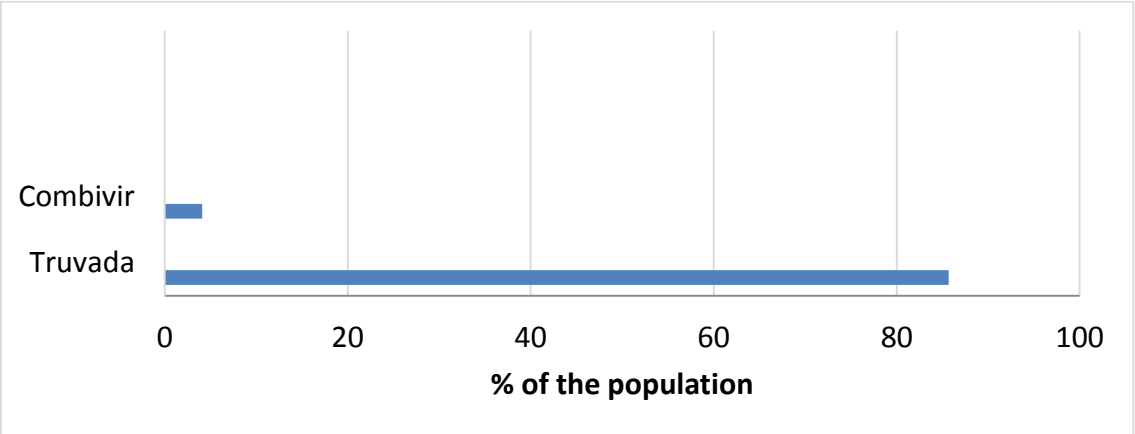

Figure 13a: The distribution of the main drugs which HIV positive people use

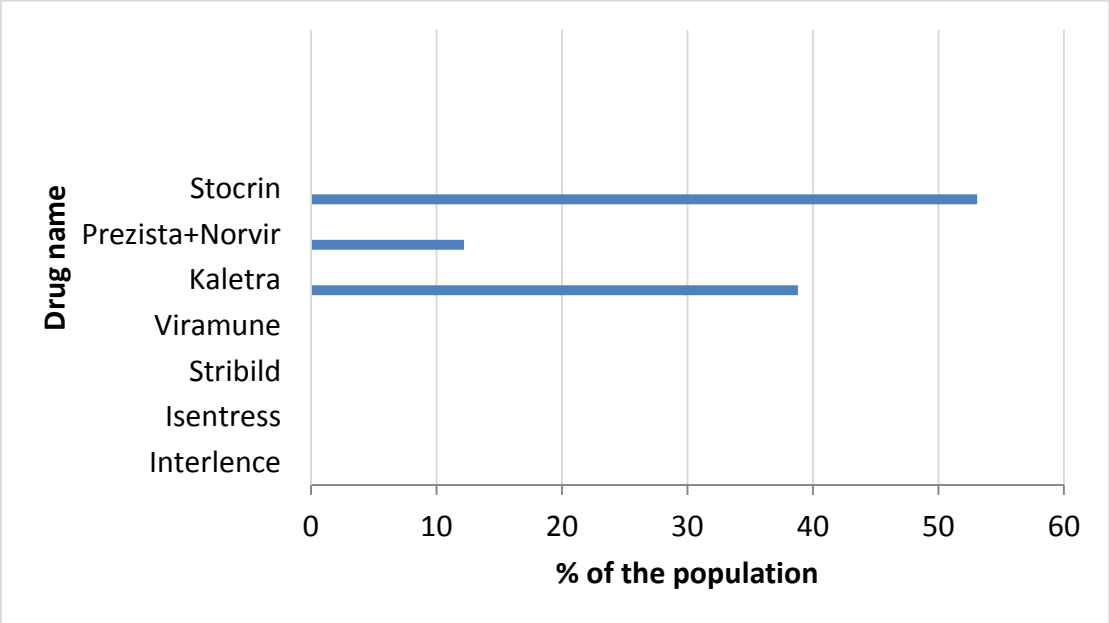

Figure 13b: The distribution of complementary drugs which HIV positive people use

Standard antiretroviral therapy (ART) consists of the combination of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop the progression of HIV disease. There's very good evidence that the HIV treatment

available today will work against the virus in the long term and keep the viral load undetectable indefinitely.

However, for this to be the case, it's very important to take the HIV treatment properly. Adherence is the most important factor under control in the success of HIV treatment. Not taking HIV treatment properly can mean that the levels of the drugs in the blood are not high enough to properly fight HIV. If this happens, HIV will be able to reproduce. The strains of HIV that reproduce when taking HIV treatment can develop resistance to the drugs are taking. Resistance can mean that HIV treatment won't work effectively. Treatment not working is likely to mean that the viral load will increase and the CD4 cell count, an important indicator of the health of the immune system, will fall. This situation increases the chances of becoming ill because of the human immunodeficiency virus. If the viral load increases to detectable levels, there may be need to change the HIV treatment. The new treatment might be more difficult to take than the combination taking before and could involve a risk of more, or new, side-effects.

In figure 13a and 13b the drug types are summarized. The 85,7% of the population using as a combination drug "Truvada". It is a tablet comprising drug which contains 200 mg emtricitabine and 245 mg tenofovir. Common side effects are nausea, diarrhoea, headache, raised creatine kinase levels, skin darkening. Rare side effects are lactic acidosis, liver damage. These side effects can affect the food consumption and directly the nutritional status.

Secondly as a complementary drugs are summarized in figure 13a mostly used drugs are "Stocrin" which is non-nucleoside reverse transcriptase inhibitors (NNRTIs). Common side effects are rash, dizziness, sleep disturbance, abnormal dreams, impaired concentration, nausea, vomiting, headache, tiredness, diarrhoea, anxiety, depression, suicidal thoughts and the rare side effects are psychosis, severe rash, and liver problems. Each side-effect can explain why the nutritional problems come out.

In this study, mostly used drugs are "Kaletra" (38,8%) and "Prezista+Norvir" (12,2%). These are the protease inhibitor type drugs. The major side effects are lipodystrophy,

raised liver enzymes, nausea, vomiting, diarrhoea, abdominal pain, weakness, heartburn, headache, raised lipids, liver toxicity, and diabetes. (FDA, 2014)

In a cohort study which has done with 1500 patient the majority of study participants (89%) were on ART, with most (63%) on protease inhibitors. (Messina, 2014)

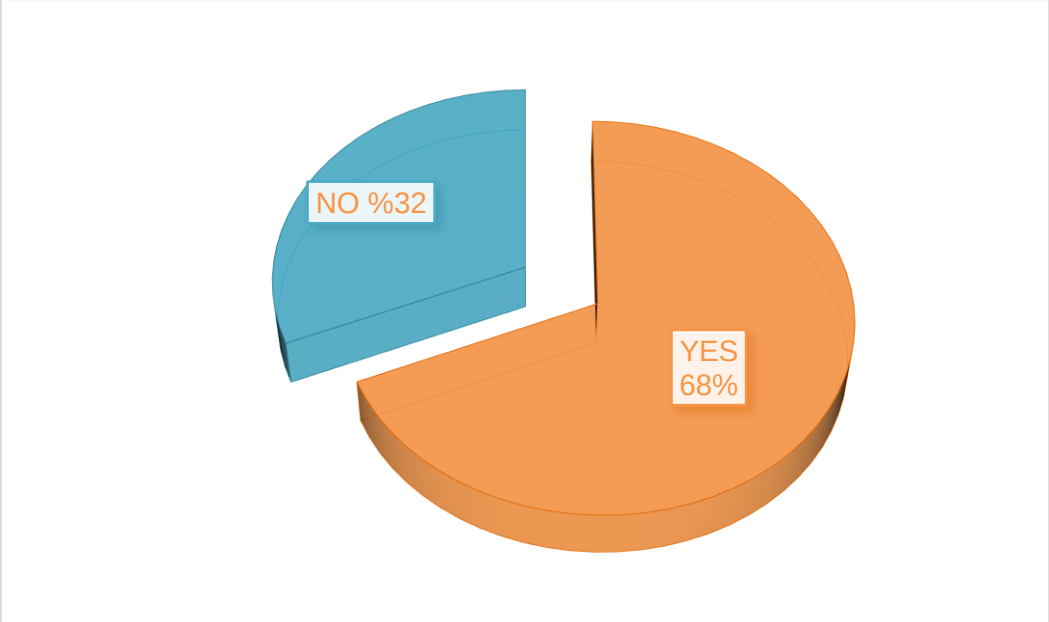

Figure 14: Drug resistance testing

As it shown in figure 14, the 68% of the study population has the drug resistance test. The 32% of the population has not the drug resistance test. It is very important that taking this test because it helps to direct the medical therapy and the drug selection. Current studies suggest a 6%–16% prevalence of HIV drug resistance in ART-naive patients, and some studies suggest that the presence of transmitted drug-resistant viruses may lead to suboptimal virologic responses. Therefore, pretreatment genotypic resistance testing should be used to guide selection of the most optimal initial ARV regimen. (U.S Department of Health and Human Service, 2012)

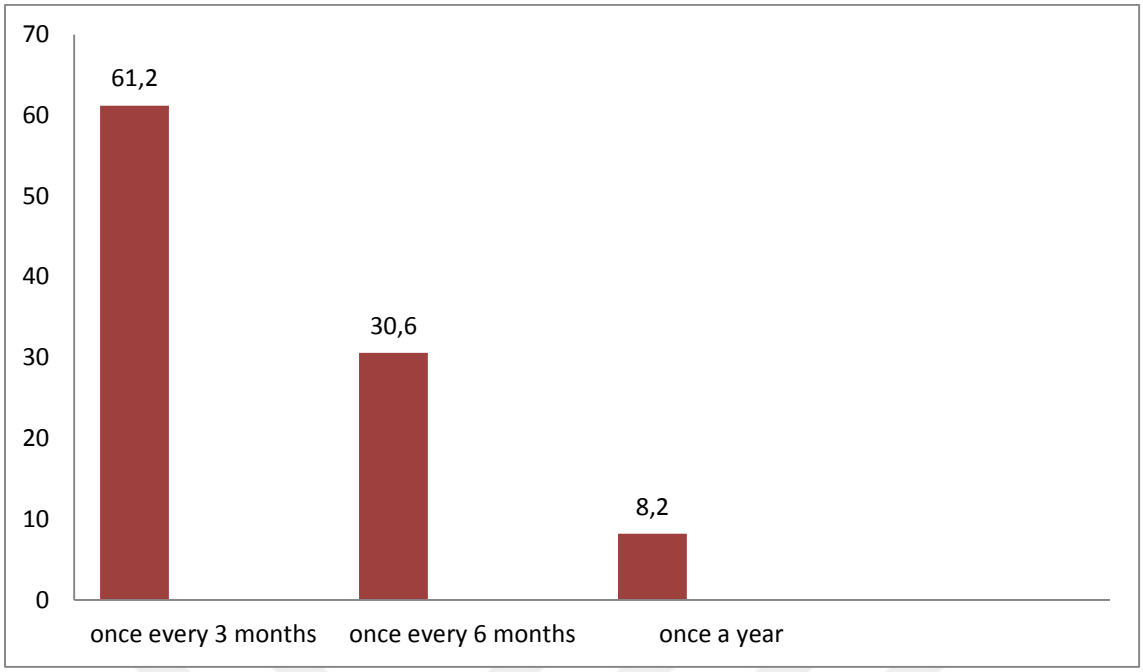

Figure 15: routine test percentages

People who has their routine tests once every 3 months are 61,2% of the population. The30, 6 % of the population has their tests once every 6 months and the 8,2% of the population has the routine tests once a year. The routine test repeating depends on the period of HIV. The hospitals and the counseling center helps and inform about the routine tests.

In figure 15, most of the population (62.5%) having their routine test every 3 months. And the same part of this population did the drug resistance test in their life. The part of the population which has no drug resistance test and doesn't get the routine tests might have some economical, social, or physical problems. The availability to the health care services might be the problem, too.

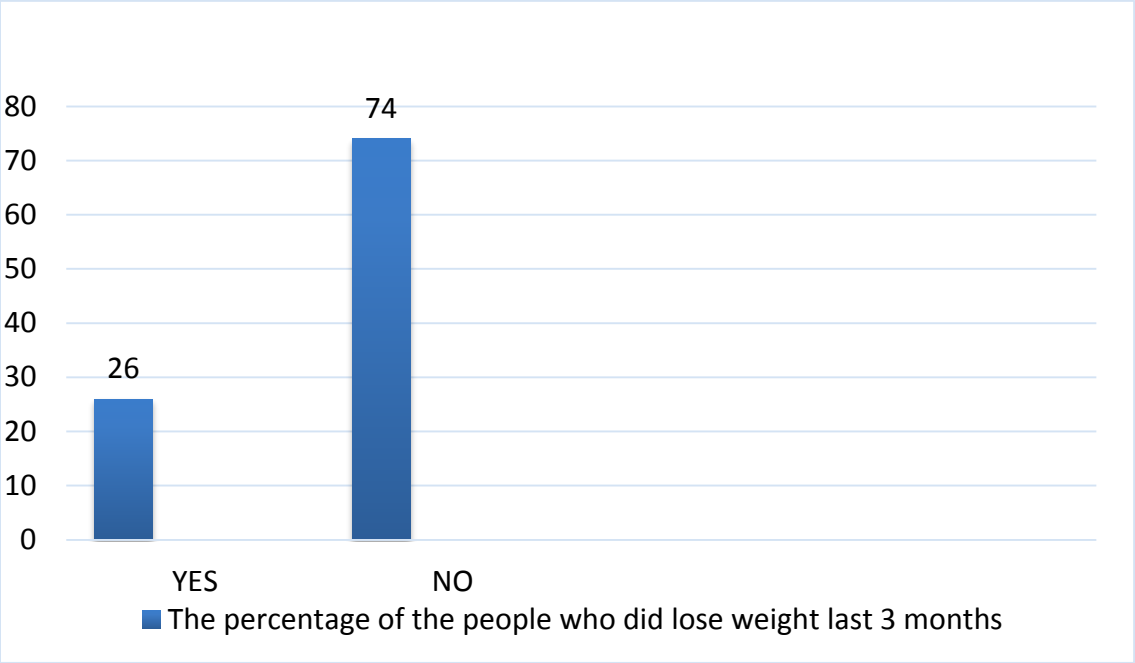

Figure 16: The percentage of people who did lose weight last 3 months.

People who lost weight last 3 months are the 26% of the population. The other 74% of the population answered as “no” to this question. Losing weight has a lot of means during the HIV infection. The weight loss is being used one of the HIV/AIDS defining diagnose.

When we look at the BMI values of who lost weight in 3 months, the average BMI value of them is 23.7 kg/m^2 (± 2.7). The 38.4% of them is still overweight and the 61.6% of them has normal BMI value despite of the weight lost.

30, 7% of the group, who lost weight in 3 months, living with HIV less than 1 year, the 53,8% of them is living with HIV 1-3 years, and the 15,3% of them has the HIV infection about 4-5 years. They are all in the asymptomatic period of HIV.

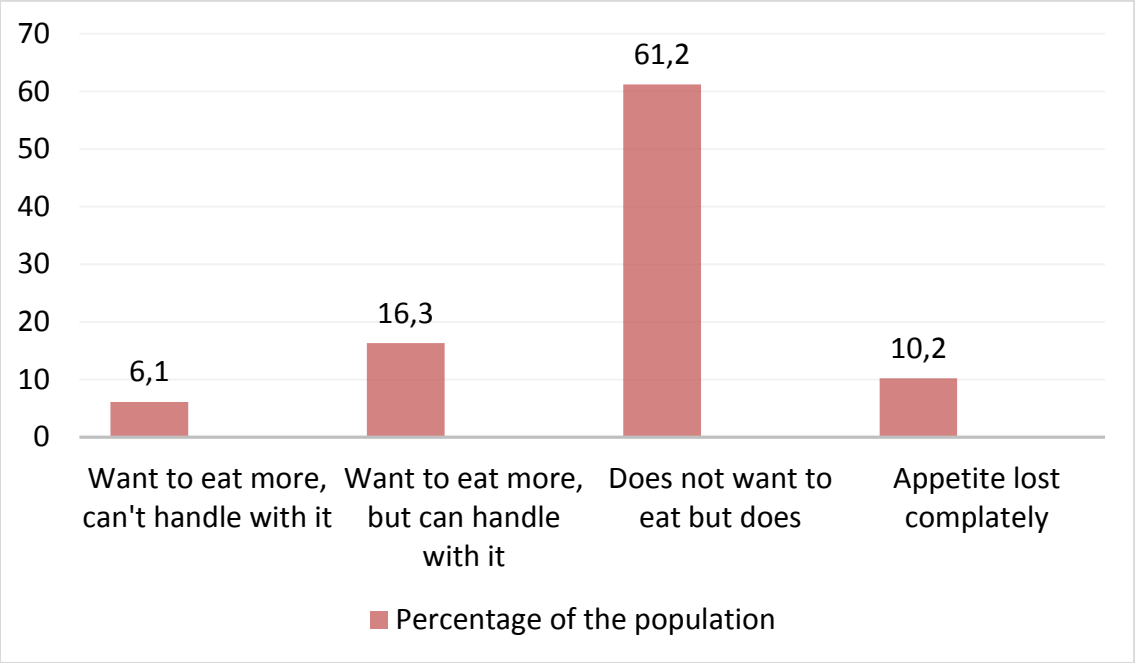

Figure 17: the appetite status of the population

When we look at the appetite status of the population, we see the 61,2% of them doesn't want to eat and they force themselves to eat. Losing appetite is one of the reasons of losing weight. If the person who doesn't want to eat or don't eat should promote for eating. Especially the nutrients which contain high energy-high protein can help. The 10,2% of the population says the appetite lost completely.

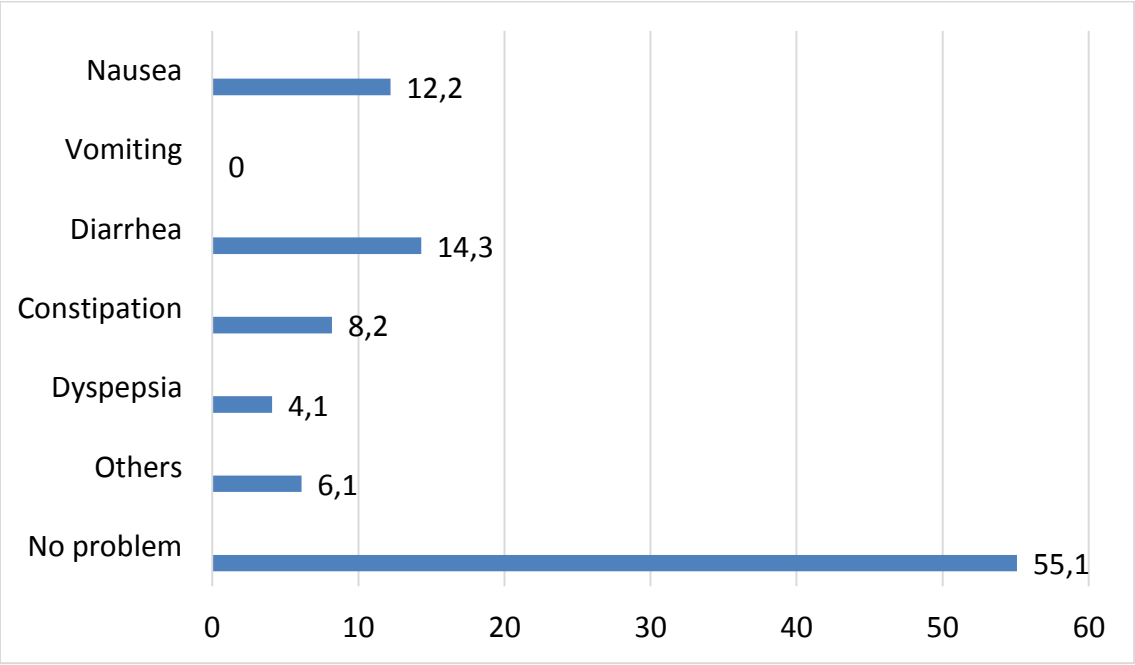

Figure 18: Digestive problems in the population

More than half of the population (55,1%) says there is no digestive problem in their digestive system. When we look at the figure 17 and figure 18 there is a high percentages of weight lost and most of them doesn't want to eat. With the Antiretroviral therapy, the drugs' major effect is nausea and diarrhea. Although the highest percentages has these two heading in figure 19, more than half of the population has no digestive problems.

There are 21 people (45,9%) who has digestive problems. And 13 people (26%) who lost weight in last 3 months. When we analyzed both informations, it is seen that 7 people are both has digestive problems and weight loss. These 7 people means 54% (13/7) of who has weight lost and 30% (21/7) who has digestive problems.

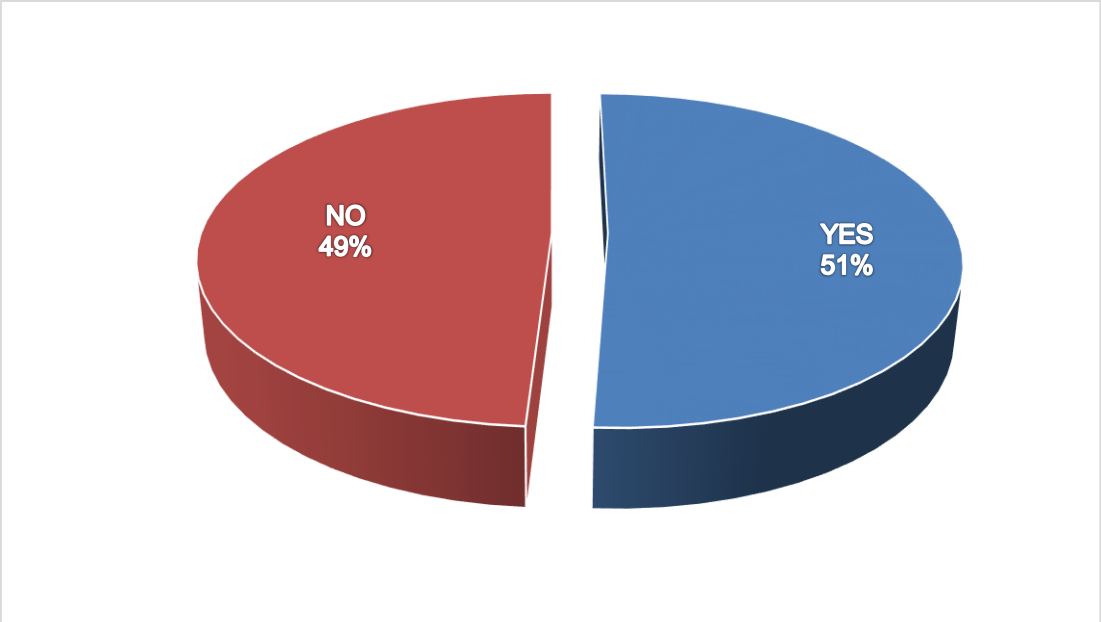

Figure 19: Supplement using

In this study 51% of the population says they use nutritional supplements. The supplements they use are mostly the complex vitamins, or only vitamin C, B12 and vitamin D. As a mineral supplementation, mostly the selenium is being used. Also the fish oil has a common usage.

The 54% of the population, who lost weight in 3 months, uses supplements.

After infected with HIV, during the ART, the body gets weaker and open to the other infections. The period of ART should be support with a good nutrition. According to the studies good nutrition can delay time to HAART and affect response to HAART. (Chandrasekhar, 2011)

For drug users, Ever-IDUs had lower total, soluble, and insoluble fiber and individual micronutrient intakes. A higher proportion of ever-IDUs had hepatitis C and HIV-related symptoms, used highly active antiretroviral therapy (HAART) less, and had a CD4 count <500 cells/mm3, than never-IDUs (Hendricks, 2010)

In Safihan, anthropometric indices and dietary intake in HIV-Infected patients were studied. Low nutrient intake was not seen in men however, women had low intake of vitamin B12, folate and vitamin E compared to RDA. However, the amount of vitamin B12 among infected men and energy intake among infected women were lower than Isfahanian healthy population's intake. (Iraj Karimi et al., 2010)

In Indıa, nutritional status of 50 HIV positive female were studied. Statistically it was found in the age group 25-30 years and 30-35 years. Statistically it was found that as age advances occurrence of HIV/AIDS decreases. In most of the subjects low socioeconomic status category, apparent inadequate food intake and caloric deficiency was observed. The majority of subjects were non-vegetarian but then also protein deficiency was observed. Moderate to severe macro and micronutrient deficiencies were observed in almost all cases. 39.27% showed less intake of vitamin A. (Sarika Gaikwad and Kalpana Jadhav, 2010)

Nutritional supplementation is a feasible method to restore food energy intake in HIV-infected patients with recent weight loss. Benefits of nutritional supplementation included a significant increase in body weight, correcting changes in body composition and improving immune function in HIV-positive patients that present at ART initiation with weight loss. Additional benefits of nutritional supplementation include reversing malnutrition, reducing inflammation or severity of anemia (improvement in red blood cell count and hemoglobin levels) and improving physical activity, thereby improving quality of life and ultimately reducing HIV-associated complications. Larger studies with long-term follow-up are necessary to validate these data. (Evans, 2013)

Table 13: Who they have their meals with

Meals	Alone%	Family%	Friends%
Breakfast	62,2	25,5	12,2
Lunch	47,9	6,1	45,9
Dinner	34,7	44,9	20,4
Average	48,3	25,5	26,2

People generally eat more when they are alone. With this information we can compare the consumption of daily energy percentages according to the meals. In table 13, the 48,3% of the population eats most meals alone, 25,5% of them eats with family and the other 26,2% eats with their friends.

4. CONCLUSION

For more than two decades now, the acquired immune deficiency syndrome and its etiological agent, the human immunodeficiency virus (HIV/AIDS) has been a growing challenge that affects all segments of global population.

When ART has been established and malnutrition treated, the nutritional quality of the diet and quality of food is important because of the long term metabolic effects of ART (dyslipidemia, insulin resistance, obesity).

The etiology of HIV-associated wasting is multifactorial, and causes may include socioeconomic status, access to care, cultural practices, psychological factors, and medical complications of and therapies for HIV infection. We can categorize these into 2 main categories: decreased nutrient intake and altered nutrient metabolism.

Generally, the study population has normal BMI value. Most of the population (55.1%) has not digestive problems. And even if they don't want to eat the meals, they do. That may be the explanation of normal BMI. The lean body mass and the fat mass percentages are not available. Plus this, the biochemical laboratory results are not available either. So the normal BMI value doesn't mean people have no problem or they live healthily.
On the other hand, there is another individual group who has some digestive problems like. It can help to explain the 10 to 49 (20%) people of the population lost weight last 3 months.

The BMI analyzes showed that he most of the population (35 individuals) has normal BMI value and most of them (18 individuals) are living with HIV about 2-3 years. Normal BMI value means no healthy body. The lean body mass and lipid profile should be analyzed at the same time.

However we see the BMI results are normal, the caloric intake is lower than the DRI values. Maybe the basal metabolic rate is lower than we calculated. So they do not lose weight despite of the inadequate caloric intake. Or the physical activity which we foreseen is high who is living sedentary life. So they don't need the energy we calculated.

Also the psychological state of the study population could be depressive so even if they say ‘I don’t want to eat, but I do’ they may be eat less than they thought. It is also the cause of low caloric intake and low basal metabolic rate.

And the study population’s HIV stage has a deep density which is called ‘asymptomatic period- 1-3 years’. The DRI values which is foreseen for the study population is calculated for increased metabolism rate or catabolic period. So if the symptoms are not seen yet, the increased metabolism is an unexpected situation. It can also explain the inadequate caloric intake but normal BMI value.

When we analyze the population, who lost weight in 3 months, we see that 38.4% of them is still overweight and the 61,6% of them still has a normal BMI value even though their weight lost. It can be thought that the general study population had an overweight or normal BMI value before they infected with HIV.

Our results showed that HIV positive peoples’ food and energy consumption is not enough to prevent losing weight or fight for the infection’s catabolic period. The drugs and their side effects must be support with supplements and healthy foods.

Drug-nutrient interactions should be considered. In addition, many of the antiretroviral drugs and medications used to treat illness or symptoms related to HIV infection may cause nausea, anorexia, abdominal pain, diarrhea, dry mouth, and alterations in taste. The adverse effects of medication and their administration schedules on intake should be considered.

Specialized nutrition support indicated before the onset of malnutrition, because undernutrition will complicate the disease course for patients with HIV infection and AIDS.

Vitamin and mineral supplementation should be provided so the dietary intake of vitamins and minerals 1-5 times to RDA. Megadoses (10 times to RDA) are discouraged. Routine monitoring and supplementation of selected of micronutrients (calcium, vitamin A, vitamin E, folate, Vitamin B12, iron , zinc) are recommended.

The 51% of the study subject said they got enough counseling from the hospitals or counseling center. That percentage is not enough to say there is enough counseling centers around them. Counseling centers should be supported by the government. And there should be both HIV positive individuals and health workers such as doctors and dietitians.

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Appendix

1. Survey

Açıklama: Bu çalışmaya gönüllü olarak katılan sizlerin tıbbi tedavisinde hiç bir değişiklik yapılmayacaktır. Araştırmanın size veya tedavinize bir zararı dokunmayacaktır. Anket sonuçları toplu olarak analiz edilip raporlanacağı için isminiz ve kurumunuz hiçbir şekilde gerekmemektedir. Desteğiniz için teşekkür ederiz.

AĞIRLIK: ..... kg BOY : ..... cm YAŞ: .....Cinsiyet: □ E □ K

1. HIV ile enfekte olma süreniz:

- □ 1 yıldan az
- □ 1-3 yıl
- □ 3-5 yıl
- □ 5-10 yıl
- □ 10-15 yıl
- □ 15-20 yıl
- □ 20-30 yıl
- □ 30 yıldan fazla

2. HIV Pozitif olduğunuzu hangi test ile öğrendiniz?

- □ Anti HIV (P24 Ab/Ag)
- □ Hızlı kart test
- □ Diğer:.....

3. HIV Elisa testi pozitif sonucu aldığınızda aşağıdaki teslerden hangisi ya da hangilerini yaptırdınız? Hangilerinden pozitif sonuç aldınız?

- □ HIV Doğrulama (Western Blot)
- □ HIV RNA (HIV PCR)

4.HIV pozitif sonucunuzu öğrendiğinizde yeterli danışmanlık hizmeti aldığınızı düşünüyor musunuz?

- □ Evet
- □ Hayır

5.Kullanmakta olduğunuz ilaçlar hangisi ya da hangileridir? (Birden fazla seçenek işaretleyebilirsiniz)

- Truvada
- Combivir

- Kaletra
- Prezista+Norvir
- Viramune
- Stocrin
- Stribild
- Isentress
- Intelence

Diğer: .....

6.İlaç direnç testlerini yaptırdınız mı?

- Evet
- Hayır

7.Rutin testlerinzii hangi sıklıkta yaptırıyor sunuz?

- 3 ayda bir
- 6 ayda bir
- Yılda bir
- Daha fazla .....

8. Son 3 ay içinde istemsiz ağırlık değişimi var mı?

- EVET.....Kg artış/azalma
- HAYIR

9. İştah durumunuzu nasıl değerlendirirsiniz?

- Çok iştahlıyım, kendimi kontrol edemiyorum
- Çok iştahlıyım ama kendimi sınırlandırılyorum
- İştahım normal
- Pek iştahım yok, kendimi zorlayarak besin tüketiyorum
- Hiç iştahım yok, besinleri görmek bile istemiyorum

10. Herhangi bir sindirim probleminiz var mı?

- Bulantı
- Kusma
- İshal
- Kabızlık
- Hazımsızlık
- Diğer.....

11. Herhangi bir besin desteği (vitamin, mineral , balık yağı, protein tozu, bitkisel ürünler vb.) alıyor musunuz?

- EVET (lütfen belirtiniz) .....
- HAYIR

12. Bireyler yalnız başlarına öğün tükettiğinde normalden daha az veya aşırı beslenme davranışı gösterebilirler.

Öğünlerinizi genellikle kim/kimler ile tüketirsiniz?

KAHVALTI ☐ YALNIZ ☐ AİLE ☐ ARKADAŞ ☐ DİĞER.....

ÖĞLE ☐ YALNIZ ☐ AİLE ☐ ARKADAŞ ☐ DİĞER.....

AKŞAM ☐ YALNIZ ☐ AİLE ☐ ARKADAŞ ☐ DİĞER.....

13. SON 24 SAAT İÇİNDE TÜKETİLEN BESİNLER:

ANKET			
ÖĞÜNLER	**BESİNLER**	**MİKTARLAR***	**NOT****
SABAH			
KUŞLUK			
ÖĞLE			
İKİNDİ			
AKŞAM			
GECE			

*** Lütfen miktarları 1 su bardağı, çay bardağı, yemek kaşığı, orta boy kase vb. olarak belirtiniz **Detaylı bilgi için kullanabilirsiniz.**

2: Ethics Committee Approval

YEDİTEPE ÜNİVERSİTESİ HASTANESİ

YEDİTEPE ÜNİVERSİTESİ KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

KURUL ADI	**YEDİTEPE ÜNİVERSİTESİ KLİNİK ARAŞTIRMALAR ETİK KURULU**
AÇIK ADRES	YEDİTEPE ÜNİVERSİTESİ HASTANESİ Devlet Yolu Ankara Cad. No: 102-104, 34752 Kozyatağı, İstanbul
TELEFON	0216 578 47 97
E-POSTA	gulin.demir@yeditepe.edu.tr

BAŞVURU BİLGİLERİ	ARAŞTIRMANIN AÇIK ADI	HIV Pozitif Bireylerde Beslenme Durumunun Saptanması			
	ARAŞTIRMA PROTOKOLÜNÜN KODU				
	EUDRACT NUMARASI				
	SORUMLU ARAŞTIRMACI ÜNVANI/ADI/SOYADI	Diyetisyen Burcu Yavunç			
	SORUMLU ARAŞTIRMACININ UZMANLIK ALANI	Diyetisyen			
	KOORDİNATÖRÜN ÜNVANI/ADI/SOYADI				
	KOORDİNATÖRÜN UZMANLIK ALANI				
	ARAŞTIRMA MERKEZİ	POZİTİF YAŞAM DERNEĞİ			
	ARAŞTIRMA MERKEZİNİN AÇIK ADRESİ	POZİTİF YAŞAM DERNEĞİ			
	DESTEKLEYİCİ VE AÇIK ADRESİ				
	DESTEKLEYİCİNİN YASAL TEMSİLCİSİ VE ADRESİ				
	UZMANLIK TEZİ/AKADEMİK AMAÇLI	UZMANLIK TEZİ ☒	AKADEMİK AMAÇLI ☐		
	ARAŞTIRMANIN FAZI VE TÜRÜ	FAZ 1 ☐			
		FAZ 2 ☐			
		FAZ 3 ☐			
		FAZ 4 ☐			
		BE/BY ☐			
		DİĞER ☐	Diğer ise belirtiniz:		
		İLAÇ ARAŞTIRMA DIŞI ☒	Belirtiniz:Genetik çalışma		
	ARAŞTIRMAYA KATILAN MERKEZLER	TEK MERKEZ ☐	ÇOK MERKEZLİ ☒	ULUSAL ☒	ULUSLARARASI ☐

	Belge Adı	Tarihi	Versiyon Numarası	Dili
DEĞERLENDİRİLEN BELGELER	ARAŞTIRMA PROTOKOLÜ			Türkçe ☒ İngilizce ☐ Diğer ☐
	ARAŞTIRMA BROŞÜRÜ			Türkçe ☐ İngilizce ☐ Diğer ☐
	BİLGİLENDİRİLMİŞ GÖNÜLLÜ OLUR FORMU			Türkçe ☒ İngilizce ☐ Diğer ☐
	OLGU RAPOR FORMU			Türkçe ☒ İngilizce ☐ Diğer ☐

	Belge Adı		Açıklama
DEĞERLENDİRİLEN DİĞER BELGELER	ARAŞTIRMA BÜTÇESİ	☐	
	SİGORTA	☐	
	HASTA KARTI/GÜNLÜKLERİ	☐	

YEDİTEPE ÜNİVERSİTESİ HASTANESİ

YEDİTEPE ÜNİVERSİTESİ KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

	İLAN	☐	
	YILLIK BİLDİRİM	☐	
	SONUÇ RAPORU	☐	
	GÜVENLİLİK BİLDİRİMLERİ	☐	
	DİĞER	☐	

KARAR BİLGİLERİ	**Karar No:** 434	**Tarih:03.06.2014**
	Burcu Yavunç sorumluluğunda yapılması tasarlanan ve yukarıda başvuru bilgileri verilen klinik araştırma başvuru dosyası ve ilgili belgeler araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş, gerçekleştirilmesinde etik bir sakınca bulunmadığına toplantıya katılan etik kurulu üyelerinin oy çokluğu ile karar verilmiştir.	

ETİK KURULU BİLGİLERİ

ÇALIŞMA ESASI	Klinik Araştırmalar Hakkında Yönetmelik, İyi Klinik Uygulamaları Kılavuzu, Yeditepe Üniversitesi Tıp Fakültesi, Klinik Araştırmalar Etik Kurulu Kuruluş ve Çalışma Esasları.

ETİK KURUL BAŞKANI UNVANI/ADI/SOYADI: Prof. Dr. R. Serdar ALPAN

ETİK KURULU ÜYELERİ

Unvanı/Adı/Soyadı	Uzmanlık Alanı	Kurumu	Cinsiyet		İlişki *		Katılım **		İmza
Prof. Dr. R. Serdar Alpan	Farmakoloji	YÜTF	E ☒	K ☐	E ☐	H ☐	E ☐	H ☐	
Prof. Dr. M. Reha Cengizlier	Pediatri	YÜTF	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Serdar Öztezcan	Biyokimya	YÜTF	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Baki Ekçi	Genel Cerrahi	YÜTF	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Ferda Özkan	Patoloji	YÜTF	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Prof. Dr. Nural Bekiroğlu	Biyoistatistik	MÜTF	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Esra Can Say	Diş Has. Ted.	YÜDF	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Doç. Dr. Meriç Köksal	Eczacılık	YÜEF	E ☐	K ☒	E ☐	H ☐	E ☐	H ☐	
Prof. Dr. Ali Rıza Okur	Hukuk	YÜHF	E ☒	K ☐	E ☐	H ☐	E ☐	H ☐	
Prof.Dr. Başar Atalay	Beyin Cerrahi	YÜTF	E ☒	K ☐	E ☐	H ☒	E ☒	H ☐	
Doç.Dr.Nesrin Sarıman	Göğüs Hastalıkları	MÜTF	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Yrd.Doç.Dr.Esin Öztürk Işık	Biyomedikal Mühendisi	YÜTF	E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	
Yakut Gümüşlügil	Sivil Üye		E ☐	K ☒	E ☐	H ☒	E ☒	H ☐	

* : Araştırma ile İlişki
** : Toplantıda Bulunma

Önemli Not: Çalışmanızın Klinik Araştırmalar Etik Kurulu tarafından onaylanan protokole göre yürütülmesi ve çalışma protokolündeki değişiklilerin kurulumuza bildirilmesi gerekmektedir.

Appendix 3: CV

Adı Soyadı: Burcu Yavunç

Doğum Tarihi: 01.01.1990

Unvanı: Diyetisyen

Öğrenim Durumu: Yüksek Lisans

Derece	**Alan**	**Kurum**	**Yıl**
Lise	Fen-Matematik Bölümü	Hüseyin Avni Sözen Anadolu Lisesi	2004-2008
Lisans	Beslenme ve Diyetetik	T.C. Yeditepe Üniversitesi	2008-2012
Yüksek lisans	Beslenme ve Diyetetik	T.C. Yeditepe Üniversitesi	2012-

1. **Akademik Unvanlar**

Yüksek lisans burslu öğrenci Yeditepe Üniversitesi Beslenme ve Diyetetik Bölümü (2012-2014)

2. **Son iki yılda verdiğiniz lisans ve lisansüstü düzeydeki dersler:** Asistanlığı yapılan derslerdir. Laboratuvar ve soru çözümleri dersleri verilmiştir.

Akademik yıl	Dönem	Dersin adı	Haftalık saati		Öğrenci sayısı
			Teorik	Uygulama	
2013	Güz	Mikrobiyoloji		6	200
2013	Bahar	Besin Mikrobiyolojisi		2	45
2013	Güz	Ana çocuk beslenmesi		4	75
2013	Bahar	Çocuk Hastalıklarında Beslenme		4	75
2013	Güz	Beslenme İlkeleri		2	70

2013	Bahar	Besin Hazırlama ve Pişirme Teknikleri		8	80
2014	Güz	Ana çocuk beslenmesi		4	45