A STUDY OF ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS

Dissertation Submitted for

MD Degree (Branch I) General Medicine
March 2010

The Tamilnadu Dr.M.G.R. Medical University
Chennai – 600 032.

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CERTIFICATE

This is to certify that this dissertation titled "**A STUDY OF ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS"** submitted by **DR.R.RAGUNATHAN** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I**, Dr.R.RAGUNATHAN,** solemnly declare that the dissertation titled "**A STUDY OF ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS"** has been prepared by me. This is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai,** in partial fulfillment of the regulations for the award of MD degree (branch I) General Medicine.

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ACKNOWLEDGEMENT

At the outset, I thank our Dean **Dr. S.M.SHIVAKUMAR, M.S.,** for permitting me to use the facilities of Madurai Medical College and Government Rajaji Hospital to conduct this study.

I wish to express my respect and sincere gratitude to my beloved teacher and Head of the Department of Medicine, **PROF.A.AYYAPPAN, M.D.,** for his valuable guidance and encouragement throughout the study and also during my post graduate course. I owe my sincere thanks to him.

I express my special thanks to my unit chief, **DR. M.NATARAJAN, M.D.**

I am greatly indebted to my beloved teachers, **Dr.Daniel. K. Moses,M.D., Dr.S.Vadivel murugan.,M.D, Dr.D.D.Venkatraman M.D., Dr.M.Muthiah, M.D., Dr. V.T.Premkumar M.D., Dr.J.Sangmani, M.D.,**

I am extremely thankful to my unit Assistant Professors**,Dr.V.N.Alaga venkatesan,M.D**, **Dr.K.Murali dharan,M.D.**

My sincere thanks to my former chief **DR.M.Kamaraj.M.D**., and Assistant Professors **Dr.S.Sooriyakumar,M.D., Dr.C.Dharmaraj,M.D., Dr.Manimegalai.M.D.** for their constant encouragement, timely help and critical suggestions throughout the study and also for making my stay in the unit both informative and pleasurable.

I profusely thank the Biochemistry, STD Departments for their cooperation and support.

I extend my thanks to my family and friends who have stood by me during my times of need. Their help and support have been invaluable to the study.

Finally, I thank all the patients, who form the most integral part of the work, and were always kind and cooperative. I pray for their speedy recovery and place this study as a tribute to them.

CONTENTS

INTRODUCTION

AIDS was first recognized in the United States in the summer of 1981, when the U.S. Centers for Disease Control and Prevention (CDC) reported the unexplained occurrence of Pneumocystis jiroveci (formerly P. carinii) pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma (KS) with or without P. jiroveci pneumonia in 26 previously healthy homosexual men in New York and Los Angeles. Within months, the disease became recognized in male and female injection drug users (IDUs) and soon thereafter in recipients of blood transfusions and in hemophiliacs. As the epidemiologic pattern of the disease unfolded, it became clear that an infectious agent transmissible by sexual (homosexual and heterosexual) contact and blood or blood products was the most likely etiologic cause of the epidemic[1].

In 1983, human immunodeficiency virus (HIV) was isolated from a patient with lymphadenopathy, and by 1984 it was demonstrated clearly to be the causative agent of AIDS. In 1985, a sensitive enzyme-linked immunosorbent assay (ELISA) was developed, which led to an appreciation of the scope and evolution of the HIV epidemic at first in the

United States and other developed nations and ultimately among developing nations throughout the world [1.]

Luc Montaineger from Pasteur Institute, France, discovered the causative agent in 1983,and labelled it as LAV -2 lymphadenopathy associated virus.[2]. Robert Gallo from USA also isolated the virus in 1984, and named it HTLV-III, Human T Lymphotropic Virus-III. The International committee on Taxonomy of Viruses re designated both the viruses and named it as Human Immunodeficiency Virus.

Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV) which can be contracted through sexual contact, exposure to blood including sharing contaminated needles and syringes and by certain blood products or other body fluids. Human immunodeficiency virus/acquired immunodeficiency syndrome has been the leading cause of death among young adults in the United state and has a devastating impact on people in the developing countries[2]. The clinical presentation of this disease include pneumonia, fever/pyrexia loss of vision, night sweats, chronic diarrhoea, weight loss, lymphadenopathy, cough, and itchy maculopapular generalized skin rash, blue discolouration, anaemia and hairy leukoplakia. [3,4,5,6]

Worldwide there are an estimated 33 million persons infected with HIV. In Central and East Africa in some urban areas, as many as one-third of sexually active adults are infected. HIV infection began to spread in Asia in the late 1980s. The most common mode of transmission is bidirectional heterosexual spread. The reason for the greater risk for transmission with heterosexual intercourse in Africa and Asia than in the United States may relate to cofactors such as general health status, the presence of genital ulcers, relative lack of male circumcision, the number of sexual partners, and different HIV serotypes[7].

Incidence in India

In 2006, the Joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimated that 5.7 million people in India were infected with the human immunodeficiency virus (HIV), a figure that captured wide attention and raised the possibility that India had more infected people than any other country[10].In 2007, however, the estimate was revised downward to 2.5 million (range, 2.0 million to 3.1 million) - a revision so large that it reduced by nearly 10%[10] .

The staggering worldwide evolution of the HIV pandemic has been matched by an explosion of information in the areas of HIV virology, pathogenesis (both immunologic and virologic), treatment of HIV disease, treatment and prophylaxis of the opportunistic diseases associated with HIV infection, prevention of infection, and vaccine development. The information flow related to HIV disease is enormous and continues to expand, and it has become almost impossible for the health care generalist to stay abreast of the literature. The purpose of this study is to present the prevalence of the electrolyte disturbances among HIV-infected patients admitted in medicine and STD Dept.'s, Govt. Rajaji Hospital, Madurai.

REVIEW OF LITERATURES

Etiologic Agent

The etiologic agent of AIDS is HIV, which belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses.. The four recognized human retroviruses belong to two distinct groups: the human T lymphotropic viruses (HTLV)-I and HTLV-II, which are transforming retroviruses; and the human immunodeficiency viruses, HIV-1 and HIV-2, which cause cytopathic effects either directly or indirectly. The most common cause of HIV disease throughout the world, and certainly in the United States, is HIV-1, which comprises several subtypes with different geographic distributions. HIV-2 was first identified in 1986 in West African patients and was originally confined to West Africa. However, a number of cases that can be traced to West Africa or to sexual contacts with West Africans have been identified throughout the world. Both HIV-1 and HIV-2 are zoonotic infections. The Pan troglodytes troglodytes species of chimpanzees has been established as the natural reservoir of HIV-1 and the most likely source of original human infection. HIV-2 is more closely related phylogenetically to the simian immunodeficiency virus (SIV) found in sooty mangabeys than it is to HIV-1[1].

Epidemiology

The modes of transmission of HIV are similar to those of hepatitis B, in particular with respect to sexual, parenteral, and vertical transmission. Although certain sexual practices (eg, receptive anal intercourse) are significantly riskier than other sexual practices (eg, oral sex), it is difficult to quantify per-contact risks. The reason is that studies of sexual transmission of HIV show that most people at risk for HIV infection engage in a variety of sexual practices and have sex with multiple persons, only some of whom may actually be HIV infected. Thus, it is difficult to determine which practice with which person actually resulted in HIV transmission[7].

Nonetheless, the best available estimates indicate that the risk of HIV transmission with receptive anal intercourse is between 1:100 and 1:30, with insertive anal intercourse 1:1000, with receptive vaginal intercourse 1:1000, with insertive vaginal intercourse 1:10,000, and with receptive fellatio with ejaculation 1:1000. The per-contact risk of HIV transmission with other behaviors, including receptive fellatio without ejaculation, insertive fellatio, and cunnilingus, is not known[7].

All per-contact risk estimates assume that the source is HIV infected. If the HIV status of the source is unknown, the risk of transmission

is the risk of transmission multiplied by the probability that the source is HIV infected. This would vary by risk practices, age, and geographic area. A number of cofactors are known to increase the risk of HIV transmission during a given encounter, including the presence of ulcerative or inflammatory sexually transmitted diseases, trauma, menses, and lack of male circumcision[7].

The risk of acquiring HIV infection from a needlestick with infected blood is approximately 1:300. Factors known to increase the risk of transmission include depth of penetration, hollow bore needles, visible blood on the needle, and advanced stage of disease in the source. The risk of HIV transmission from a mucosal splash with infected blood is unknown but is assumed to be significantly lower[7].

The risk of acquiring HIV infection from illicit drug use with sharing of needles from an HIV-infected source is estimated to be 1:150. Use of clean needles markedly decreases the chance of HIV transmission but does not eliminate it if other drug paraphernalia are shared (eg, cookers)[7,8].

When blood transfusion from an HIV-infected donor occurs, the risk of transmission is 95%. Fortunately, since 1985, blood donor screening using the HIV enzyme-linked immunosorbent assay (ELISA) has been universally

practiced in the United States. Also, persons who have recently engaged in unsafe behaviors (eg, sex with a person at risk for HIV, injection drug use) are not allowed to donate. This eliminates donations from persons who are HIV infected but have not yet developed antibodies (ie, persons in the "window" period). In recent years, HIV antigen and viral load testing have been added to the screening of blood to further lower the chance of HIV transmission. With these precautions, the chance of HIV transmission with receipt of blood transfusion is about 1:1,000,000[7].

In the absence of perinatal HIV prophylaxis, between 13% and 40% of children born to HIV-infected mothers contract HIV infection. The risk is higher with vaginal than with cesarean delivery, higher among mothers with high viral loads, and higher among those who breast-feed their children. The risk can be decreased by administering antiretroviral treatment to the mother during pregnancy and to the infant immediately after birth[7,9]. HIV has not been shown to be transmitted by respiratory droplet spread, by vectors such as mosquitoes, or by casual nonsexual contact[7].

In general, the progression of HIV-related illness is similar in men and women. However, there are some important differences. Women

seek medical attention later than men. They are at risk for gynecologic complications of HIV, including recurrent candidal vaginitis, pelvic inflammatory disease, and cervical dysplasia. Violence directed against women, pregnancy, and frequent occurrence of drug use and poverty all complicate the treatment of HIV-infected women[7].

CLINICAL MANIFESTATIONS[1]

The clinical consequences of HIV infection encompass a spectrum ranging from an acute syndrome associated with primary infection to a prolonged asymptomatic state to advanced disease.

THE ACUTE HIV SYNDROME[1]:

The acute phase represents the initial response of an immunocompetent adult to HIV infection. Clinically, this is typically a self-limited illness that develops in 50% to 70% of adults 3 to 6 weeks after infection; it is characterized by nonspecific symptoms including sore throat, myalgia, fever, rash, and sometimes aseptic meningitis.

The Asymptomatic Stage—Clinical Latency[1]

Although the length of time from initial infection to the development of clinical disease varies greatly, the median time for untreated patients is ~10 years. HIV disease with active virus replication is ongoing and progressive during this asymptomatic period.

The middle, chronic phase represents a stage of relative containment of the virus. The immune system is largely intact at this point, but there is continued HIV replication that may last for several years. Patients either are asymptomatic or develop persistent lymphadenopathy, and many patients have "minor" opportunistic infections such as thrush (Candida) or herpes zoster. During this phase, viral replication in the lymphoid tissues continues unabated. The extensive viral turnover is associated with continued loss of CD4+ cells, but a large proportion of the CD4+ cells is replenished and the decline of CD4+ cells in the peripheral blood is modest

Symptomatic Disease[1]

The final, crisis phase is characterized by a catastrophic breakdown of host defenses, a marked increase in viremia, and clinical disease. Typically, patients present with fever of more than 1 month's duration, fatigue, weight loss, and diarrhea; the CD4+ cell count is reduced below 500 cells/μL. After a variable interval, patients develop serious opportunistic infections, secondary neoplasms, and/or neurologic

manifestations (so-called AIDS-defining conditions), and the patient is said to have full-blown AIDS

A diagnosis of AIDS is made in anyone with HIV infection and a CD4+ T cell count <200/µL and in anyone with HIV infection who develops one of the HIV-associated diseases considered to be indicative of a severe defect in cell-mediated immunity .

Clinical Categories of HIV Infection[1]

Category A*:*

Consists of one or more of the conditions listed below in an adolescent or adult (>13 years) with documented HIV infection. Conditions listed in categories B and C must not have occurred.

Asymptomatic HIV infection

Persistent generalized lymphadenopathy

Acute (primary) HIV infection with accompanying illness or history of acute HIV infection

Category B:

It consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in clinical category C and that meet at least one of the following criteria:

(1) The conditions are attributed to HIV infection or are indicative of a defect in cell-mediated immunity; or

(2) the conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection. Examples include, but are not limited to, the following:

Bacillary angiomatosis

Candidiasis, oropharyngeal (thrush)

Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy

Cervical dysplasia (moderate or severe)/cervical carcinoma in situ

Constitutional symptoms, such as fever (38.5°C) or diarrhea lasting >1 month

Hairy leukoplakia, oral

Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome

Idiopathic thrombocytopenic purpura

Listeriosis

Pelvic inflammatory disease, particularly if complicated by tuboovarian abscess

Peripheral neuropathy

Category C:

Conditions listed in the AIDS surveillance case definition.

Candidiasis of bronchi, trachea, or lungs

Candidiasis, esophageal

Cervical cancer, invasive

Coccidioidomycosis, disseminated or extrapulmonary

Cryptococcosis, extrapulmonary

Cryptosporidiosis, chronic intestinal (>1 month's duration)

Cytomegalovirus disease (other than liver, spleen, or nodes)

Cytomegalovirus retinitis (with loss of vision)

Encephalopathy, HIV-related

Herpes simplex: chronic ulcer(s) (>1 month's duration); or bronchitis, pneumonia, or esophagitis

Histoplasmosis, disseminated or extrapulmonary

Isosporiasis, chronic intestinal (>1 month's duration)

Kaposi's sarcoma

Lymphoma, Burkitt's (or equivalent term)

Lymphoma, primary, of brain

Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary

Mycobacterium tuberculosis, any site (pulmonary[a] or extrapulmonary)

Mycobacterium, other species or unidentified species, disseminated or extrapulmonary

Pneumocystis jiroveci pneumonia

Pneumonia, recurrent[a]

Progressive multifocal leukoencephalopathy

Salmonella septicemia, recurrent

Toxoplasmosis of brain

Wasting syndrome due to HIV

Diagnosis and Laboratory Monitoring of HIV Infection[11]

The establishment of HIV as the causative agent of AIDS and related syndromes early in 1984 was followed by the rapid development of sensitive screening tests for HIV infection. By March 1985, blood donors in the

United States were routinely screened for antibodies to HIV. In June 1996, blood banks in the United States added the p24 antigen capture assay to the screening process to help identify the rare infected individuals who were donating blood in the time (up to 3 months) between infection and the development of antibodies. In 2002 the ability to detect early infection with HIV was further enhanced by the licensure of nucleic acid testing (NAT) as a routine part of blood donor screening.

DIAGNOSIS OF HIV INFECTION

The CDC has recommended that screening for HIV infection be performed as a matter of routine health care. The diagnosis of HIV infection depends upon the demonstration of antibodies to HIV and/or the direct detection of HIV or one of its components. As noted above, antibodies to HIV generally appear in the circulation 2–12 weeks following infection.

ANTIBODY DETECTION BY ELISA/EIA :

This is the most widely used screening method. It has a sensitivity of > 99.5 %. Hence the false positivity is also present with conditions such as influenza vaccination, hepatic disease auto antibodies. Direct solid phase anti globulin ELISA is the most commonly used method. Antigen obtained

from cell cultures and recombinant techniques represents all subtypes of both HIV 1 and HIV 2. The antigen is coated on micro titre wells and test serum is added to it. If antibody to HIV is present in the serum it binds to the antigen. After washing away the unbound serum anti human immunoglobulin bound to an enzyme is added, followed by a colour forming substrate. If the test serum contains anti HIV antibody then a photo metrically detectable colour is formed and can be read by a special ELISA reader.

The first generation ELISA tests detect the anti HIV- 1 antibodies of Ig G type using antigens derived from virus grown in cell cultures.
The second generation ELISA tests detect the anti HIV - 1 and anti HIV – 2 antibodies using recombinant antigens.

Third generation ELISA tests detect Ig M antibodies using synthetic oligo peptides.

The fourth generation ELISA tests combine detection of antibodies to HIV with detection of the p24 antigen of HIV. Hence more helpful in identifying individuals with infection during the window period.

Screening is performed with an enzyme-linked immunosorbent assay (ELISA). The current HIV test used in the United States is a combination HIV-1/HIV-2 enzyme immunoassay test kit that is also

sensitive to antibodies to HIV-2. The Centers for Disease Control and Prevention offer special tests for HIV-2 and HIV-1 non-B subtypes.

A positive screening test is confirmed by a repeat positive ELISA and a positive Western blot (presence of at least two of the following bands: p24, gp41, gp120/160).

An isolated positive ELISA result should not be reported to the patient until this result is confirmed by a Western blot. An indeterminate test is one for which the ELISA is positive but the criteria for a positive Western blot are not fulfilled. A rapid HIV-1 antibody test has been approved by the U.S. Food and Drug Administration and can be considered for use outside of traditional laboratory and clinical settings.

WESTERN BLOT

The most commonly used confirmatory test is the Western blot . This assay takes advantage of the fact that multiple HIV antigens of different,well-characterized molecular weights elicit the production of specific antibodies. These antigens can be separated on the basis of molecular weight, and antibodies to each component can be detected as

discrete bands on the Western blot. A negative Western blot is one in which no bands are present at molecular weights corresponding to HIV gene products. In a patient with a positive or indeterminate EIA and a negative Western blot, one can conclude with certainty that the EIA reactivity was a false positive. On the other hand, a Western blot demonstrating antibodies to products of all three of the major genes of HIV (*gag*, *pol*, and *env*) is conclusive evidence of infection with HIV. Criteria established by the U.S. Food & Drug Administration (FDA) in 1993 for a positive Western blot state that a result is considered positive if antibodies exist to two of the three HIV proteins: p24, gp41, and gp120/160.

Complete blood count (CBC), routine chemistry

The CD4+ T cell count is the laboratory test generally accepted as the best indicator of the immediate state of immunologic competence of the patient with HIV infection. This measurement, which can be made directly or calculated as the product of the percent of CD4+ T cells (determined by flow cytometry) and the total lymphocyte count [determined by the white blood cell count (WBC) and the differential percent], has been shown to correlate very well with the level of immunologic competence.

Patients with CD4+ T cell counts <200/microL are at high risk of disease from P. jiroveci, while patients with CD4+ T cell counts <50/microL are at high risk of disease from CMV, mycobacteria of the M. avium complex (MAC) and/or T. gondii .

Patients with HIV infection should have CD4+ T cell measurements performed at the time of diagnosis and every 3–6 months thereafter. More frequent measurements should be made if a declining trend is noted.

According to most guidelines, a CD4 T cell count <350/microL is an indication for consideration of initiating ARV therapy, and a decline in CD4+ T cell count of >25% is an indication for considering a change in therapy.

Once the CD4+ T cell count is <200/microL, patients should be placed on a regimen for P.jiroveci prophylaxis, and once the count is <50/microL, primary prophylaxis for MAC infection is indicated. As with any laboratory measurement, one may wish to obtain two determinations prior to any significant changes in patient management based upon CD4+ T cell count alone.

In patients with hypersplenism or who have undergone splenectomy the CD4+ T cell percentage may be a more reliable indication of immune function than the CD4+ T cell count. A CD4+ T cell percent of 15 is comparable to a CD4+ T cell count of 200/μL.

HIV RNA DETERMINATIONS

Facilitated by highly sensitive techniques for the precise quantitation of small amounts of nucleic acids, the measurement of serum or plasma levels of HIV RNA has become an essential component in the monitoring of patients with HIV infection. As discussed under diagnosis of HIV infection, the two most commonly used techniques are the RT-PCR assay and the bDNA assay. By utilizing more sensitive, nested PCR techniques and by studying tissue levels of virus as well as plasma levels, HIV RNA can be detected in virtually every patient with HIV infection. HIV RNA measurements are greatly influenced by the state of activation of the immune system and may fluctuate greatly in the setting of secondary infections or immunization. For these reasons, decisions based upon HIV RNA levels should never be made on a single determination. Measurements of plasma HIV RNA levels should be made at the time of HIV diagnosis and every 3–6 months thereafter in the untreated patient. In general, most guidelines

suggest that therapy be considered in patients with >100,000 copies of HIV RNA per milliliter.

HIV RNA measurements are to be done frequently to monitor therapy,which pose economic burden to many people in developing countries.Hence the need other simple clinical or laboratory parameter to monitor therapy is essential in developing countries.

HIV RESISTANCE TESTING

The availability of multiple ARV drugs as treatment options has generated a great deal of interest in the potential for measuring the sensitivity of an individual's HIV virus(es) to different ARV agents. HIV resistance testing can be done through either genotypic or phenotypic measurement

CO-RECEPTOR TROPISM ASSAYS

Two commercial assays; the Trofile assay (Monogram Biosciences) and the Phenoscript assay (VIRalliance), are available to make this determination. These assays clone the envelope regions of the patient's virus into an indicator virus that is then used to infect target cells expressing either

CCR5 or CXCR4 as their co-receptor. These assays take weeks to perform and are expensive.

Tuberculin skin test

Rapid plasma reagin (RPR) test

Toxoplasma and cytomegalovirus (CMV) immunoglobin (Ig) G and hepatitis A, B (HBsAg, HBsAb, HBcAb), and C serologie

Chlamydia/gonococcal urine/cervical probe

Cervical Papanicolaou smear (most commonly using the thin prep method)

HIV resistance testing at baseline, with treatment failure, and particularly for pregnant women

Sodium Balance

Sodium is actively pumped out of cells by the Na^+, K^+-ATPase pump. As a result, 85–90% of all Na^+ is extracellular, and the ECF volume is a reflection of total body Na^+ content. Normal volume regulatory mechanisms ensure that Na^+ loss balances Na^+ gain. If this does not occur,

conditions of Na^+ excess or deficit ensue and are manifest as edematous or hypovolemic states, respectively. It is important to distinguish between disorders of osmoregulation and disorders of volume regulation since water and Na^+ balance are regulated independently. Changes in Na^+ concentration generally reflect disturbed water homeostasis, whereas alterations in Na^+ content are manifest as ECF volume contraction or expansion and imply abnormal Na^+ balance[12].

Hyponatremia

A plasma Na^+ concentration <135 mmol/L usually reflects a hypotonic state [12]

Symptoms and Signs:

Whether hyponatremia is symptomatic depends on its severity and acuity. Chronic disease can be severe (sodium concentration less than 110 mEq/L), yet remarkably asymptomatic because the brain has adapted by decreasing its tonicity over weeks to months. Acute disease that has developed over hours to days can be severely symptomatic with relatively moderate hyponatremia. Mild hyponatremia (sodium concentrations of 130–135 mEq/L) is usually asymptomatic[13].

Mild symptoms of nausea and malaise progress to headache, lethargy, and disorientation as the sodium concentration drops. The most serious symptoms are respiratory arrest, seizure, coma, permanent brain damage, brainstem herniation, and death. Premenopausal women are much more likely than menopausal women to die or suffer permanent brain injury from hyponatremic encephalopathy, suggesting a hormonal role in the pathophysiology[13,14].

Potassium Balance

Potassium is the major intracellular cation. The normal plasma K^+ concentration is 3.5–5.0 mmol/L, whereas that inside cells is about 150 mmol/L. Therefore, the amount of K^+ in the ECF (30–70 mmol) constitutes <2% of the total body K^+ content (2500–4500 mmol). The ratio of ICF to ECF K^+ concentration (normally 38:1) is the principal result of the resting membrane potential and is crucial for normal neuromuscular function. The basolateral Na^+, K^+-ATPase pump actively transports K^+ in and Na^+ out of the cell in a 2:3 ratio, and the passive outward diffusion of K^+ is quantitatively the most important factor that generates the resting membrane potential. The activity of the electrogenic Na^+, K^+-ATPase pump may be stimulated as a result of an increased intracellular Na^+ concentration

and inhibited in the setting of digoxin toxicity or chronic illness such as heart failure or renal failure[12].

The K^+ intake of individuals on an average western diet is 40–120 mmol/d, or approximately 1 mmol/kg per day, 90% of which is absorbed by the gastrointestinal tract. Maintenance of the steady state necessitates matching K^+ ingestion with excretion. Initially, extrarenal adaptive mechanisms, followed later by urinary excretion, prevent a doubling of the plasma K^+ concentration that would occur if the dietary K^+ load remained in the ECF compartment. Immediately following a meal, most of the absorbed K^+ enters cells as a result of the initial elevation in the plasma K^+ concentration and facilitated by insulin release and basal catecholamine levels. Eventually, however, the excess K^+ is excreted in the urine. The regulation of gastrointestinal K^+ handling is not well understood. The amount of K^+ lost in the stool can increase from 10 to 50% or 60% (of dietary intake) in chronic renal insufficiency. In addition, colonic secretion of K^+ is stimulated in patients with large volumes of diarrhea, resulting in potentially severe K^+ depletion.[12]

Hypokalemia

Hypokalemia is defined as a plasma K^+ concentration <3.5 mmol/L[12] Hypokalemia is often associated with acid-base disturbances related to the underlying disorder. In addition, K^+ depletion results in intracellular acidification and an increase in net acid excretion or new HCO_3^- production. This is a consequence of enhanced proximal HCO_3^- reabsorption, increased renal ammoniagenesis, and increased distal H^+ secretion. This contributes to the generation of metabolic alkalosis frequently present in hypokalemic patients. NDI is not uncommonly seen in K^+ depletion and is manifest as polydipsia and polyuria. Glucose intolerance may also occur with hypokalemia and has been attributed to either impaired insulin secretion or peripheral insulin resistance[12].

Clinical Findings:

Symptoms and Signs:

Muscular weakness, fatigue, and muscle cramps are frequent complaints in mild to moderate hypokalemia. Smooth muscle involvement may result in constipation or ileus. Flaccid paralysis, hyporeflexia, hypercapnia, tetany, and rhabdomyolysis may be seen with severe hypokalemia (< 2.5 mEq/L). The presence of hypertension may serve

as a clue to the diagnosis of hypokalemia from aldosterone or mineralcorticoid excess[13] .

Laboratory Findings

Urinary potassium concentration is low (< 20 mEq/L) as a result of extrarenal fluid loss (eg, diarrhea, vomiting) and inappropriately high (> 40 mEq/L) with urinary losses

Hypokalemia with a The transtubular [K^+] gradient (TTKG) > 4 suggests renal potassium loss with increased distal K^+ secretion. In such cases, plasma renin and aldosterone levels are helpful in differential diagnosis. The presence of nonabsorbed anions, including bicarbonate, also increases TTKG[13,15.]

Loop diuretics may cause hypomagnesemia as well as hypokalemia[13].

The electrocardiographic changes of hypokalemia are due to delayed ventricular repolarization and do not correlate well with the plasma K^+ concentration[12]. The electrocardiogram (ECG) shows decreased amplitude and broadening of T waves, prominent U waves, premature ventricular contractions, and depressed ST segments[13,16.]

Hyperkalemia

Hyperkalemia, defined as a plasma K^+ concentration >5.0 mmol/L[12], occurs as a result of either K^+ release from cells or decreased renal loss. Clinical Features Since the resting membrane potential is related to the ratio of the ICF to ECF K^+ concentration, hyperkalemia partially depolarizes the cell membrane. Prolonged depolarization impairs membrane excitability and is manifest as weakness, which may progress to flaccid paralysis and hypoventilation if the respiratory muscles are involved. Hyperkalemia also inhibits renal ammoniagenesis and reabsorption of NH_4^+ in the TALH. Thus, net acid excretion is impaired and results in metabolic acidosis, which may further exacerbate the hyperkalemia due to K^+ movement out of cells[12].

The most serious effect of hyperkalemia is cardiac toxicity, which does not correlate well with the plasma K^+ concentration. The earliest electrocardiographic changes include increased T-wave amplitude, or peaked T waves. More severe degrees of hyperkalemia result in a prolonged PR interval and QRS duration, atrioventricular conduction delay, and loss of P waves. Progressive widening of the QRS complex and merging with the T

wave produces a sine wave pattern. The terminal event is usually ventricular fibrillation or asystole[12,17].

Fluid and Electrolyte Disorders in HIV infected patients

Disorders of Osmolality

Hyponatremia is a frequent finding among HIV-infected persons, with a reported prevalence of 30-60% in hospitalized patients[18,19].

It is a marker of severe illness that is associated with increased mortality in HIV-infected patients[20]. In a study of 96 consecutive patients with acquired immune deficiency syndrome (AIDS) or AIDS-related complex (ARC) conducted in Department of Medicine, Long Island Jewish Medical Center, New Hyde Park 11042, 31.3% patients had hyponatremia. The probability of 50% survival after diagnosis of human immunodeficiency virus (HIV) infection in the hyponatremic group was 11.5 months, as compared to 39 months for those without hyponatremia, p less than 0.001. Hyponatremia occurs commonly in ambulatory patients with ARC or AIDS, appears in patients with higher mortality and morbidity, and does not represent a terminal event. Most patients had hypovolemia and unexpectedly

high urine sodium concentration, suggesting defective renal sodium conservation[20]. In another study of 212 HIV-infected patients admitted to a large metropolitan hospital, the mortality rate for the hyponatremic group was higher than that for the normonatremic group (36.5% vs 19.7%; $p < .01$) [21].

In one study, Burton D Rose et al found that Hyponatremia and hyperkalemia are the two major electrolyte disorders that may be associated with HIV infection[38]. In addition, lactic acidosis, hyperuricemia, and hypophosphatemia have been described[38]. And they have found that the incidence of hyponatremia in hospitalized HIV-infected patients has been reported to be between 35 and 55 percent. In one prospective analysis of 167 patients with AIDS and 45 patients with ARC admitted on 269 occasions to a large metropolitan teaching hospital during a 3-month period showed Eighty-three patients (39%) had hyponatremia .Hyponatremia was present on admission during 57 hospitalizations and was associated with gastrointestinal losses and hypovolemia in 43%. When hyponatremia developed during hospitalisation, 68% of the patients were clinically euvolemic and had a syndrome consistent with inappropriate secretion of antidiuretic hormone (SIADH) [22].

The etiology and management of hyponatremia may differ according to the timing of its presentation. Volume depletion caused by diarrhea or vomiting is the usual cause of hyponatremia present at the time of hospital admission. Clinical management includes replacement of the volume deficit, along with measures to treat the underlying cause of volume depletion. In contrast, the syndrome of inappropriate antidiuretic hormone (SIADH) is the likely culprit among patients who develop hyponatremia during hospitalization[18]. SIADH is associated with common pulmonary and intracranial diseases such as Pneumocystis jiroveci pneumonia, toxoplasmosis, and tuberculosis. The initial treatment of SIADH consists of fluid restriction and treatment of the underlying infection or malignancy. Persistent release of antidiuretic hormone resulting from infections that are slow to respond to treatment also can be managed with demeclocycline at a dosage of 600-1,200 mg per day, which will inhibit the action of antidiuretic hormone on the renal tubule[23]

Potassium Disorders

Both hypokalemia and hyperkalemia are common among HIV-infected patients. Hypokalemia is usually found in the setting of gastrointestinal infections leading to vomiting or diarrhea. Amphotericin B, frequently used to treat fungal infections in patients with AIDS, can cause tubular dysfunction resulting in hypokalemia. As noted, tenofovir has been associated with proximal tubular dysfunction resulting in an electrolyte wasting state, including life-threatening hypokalemia[24,25,26]

Drug-induced hyperkalemia is common among patients receiving either high-dose trimethoprim-sulfamethoxazole or intravenous pentamidine. In a manner similar to the action of potassium-sparing diuretics such as amiloride, both drugs inhibit distal nephron sodium transport, leading to a decrease in potassium secretion[27,28]. Hyperkalemia and hyponatremia also may be a manifestation of mineralocorticoid deficiency resulting from adrenal insufficiency or the syndrome of hyporeninemic hypoaldosteronism[29,30].Acute or chronic kidney disease also may contribute to potassium retention. Adrenal causes of hyperkalemia often respond clinically to treatment of the underlying disorder, loop diuretics, or fludrocortisone.[30]

Acid-Base Disorders

Acid-base disturbances in HIV-infected patients are commonly caused by infections or drugs. Respiratory alkalosis and respiratory acidosis may occur in opportunistic infections of the lungs or central nervous system. Non anion gap metabolic acidosis may occur as a result of several different processes, including intestinal losses of bases caused by diarrhea and renal acidosis resulting from adrenal insufficiency, the syndrome of hyporeninemic hypoaldosteronism, or drug toxicity (eg, amphotericin B) [31,29,32].

High anion gap metabolic acidosis in this population results from chronic kidney disease, type A lactic acidosis caused by tissue hypoxia, and type B lactic acidosis[33].Type B lactic acidosis presents with markedly elevated blood lactate levels, possibly caused by drug-induced mitochondrial dysfunction. Affected patients show no evidence of hypoxemia, tissue hypoperfusion, malignancy, or sepsis. This disorder has been reported with use of nucleoside reverse transcriptase inhibitors such as zidovudine, didanosine, zalcitabine, lamivudine, and stavudine[34]. Although life-threatening acidosis is rare, 5-25% of treated patients may develop mildly elevated lactate levels (2.5-5 mmol/L) without acidosis. The value of screening and the predictive value of small, asymptomatic elevations in lactate are unknown[34,35]. Routine monitoring for hyperlactatemia with lactic

acid levels is not recommended, but lactic acid levels should be measured in patients who present with low bicarbonate levels, an elevated anion gap, or abnormal liver enzymes[36].

Other less common electrolyte disturbances[37]

1. hypocalcemia
2. hypercalcemia
3. hypourecemia
4. hyperuricemia
5. lactic acidosis
6. hypophosphatemia

AIMS OF THE STUDY

1) To find out the prevalence of electrolyte disturbances in HIV infected patients
2) And their correlation with CD4+ counts

MATERIAL AND METHODS

Study design : Cross sectional study

Study Population:

The cross sectional study included all 150 patients admitted in medicine and STD wards, GRH. Both male and female patients were included in this study

Place : Medicine Dept.,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

Collaborative Departments: 1) Department of Bio-Chemistry,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

2) Department of STD,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

Period of study: 6 months (Nov 1,2008 to April 30, 2009).

Sample size: 150 patients.

Selection of the study subjects:

150 patients admitted with HIV infection in the medical and STD wards, Govt. Rajaji Hospital from July to December 2008 formed the study group.

All patient's with HIV infection, admitted in both medical and dept. of STD are included in this study which includes both AIDS related complex and AIDS. Since only symptomatic patients and patients with opportunistic infections(eg. T.B meningitis, chronic diarrhea, etc.,) are getting admitted in wards, asymptomatic patients were not included in this study.

111 male and 39 female patients were included in this study. Sex distribution is shown in table 1.

TABLE 1)SEX DISTRIBUTION

		FREQUENCY	PERCENT
VALID	FEMALE	39	26.0
	MALE	111	74.0
	TOTAL	150	100.0

Most patients were newly detected and some patients received anti retro viral therapy. Separation was not done. All 150 patients were HIV-1 positive for ELISA (Enzyme Linked Immuno Sorbant Assay). Test repeated and confirmed for all patients. WESTERN BLOT could not be performed because of limited resources.

Tests for CD4+ count, blood sugar, blood urea, serum creatinine, Serum sodium, serum potassium done for all patients and were recorded properly. CD4+ count was done using flow cytometry. It was measured in Cells/µL. Blood sugar, blood urea, serum creatinine, Serum sodium, serum potassium are done by using automated analyzer.

BUN (Blood Urea Nitrogen) values were calculated by using formula (BUN=blood urea/2.13). Since impaired renal function itself can alter the

serum electrolytes, patients with elevated renal parameters were not included in this study. Patients with symptomatic and asymptomatic electrolyte disturbances were not grouped.

The etiology of the electrolyte disturbances could not be found out because of limited resources.

Consent: Informed consent was obtained

Ethical committee approval: Obtained

Financial support: Nil

Conflict of interest: Nil

Statistical tool used:

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **SPSS version 13.**

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference

between quantitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

FIGURE 1

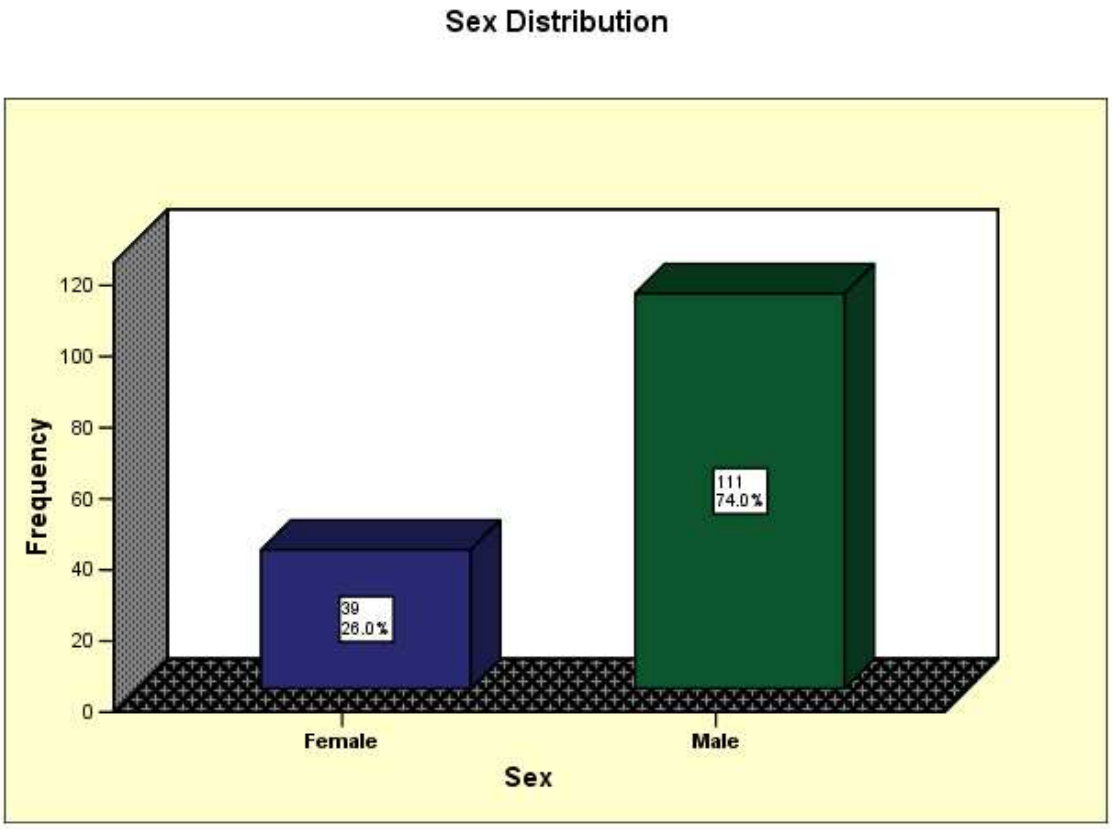

Sex Distribution
Frequency
120
100
80
60
40
20
0
39
26.0%
111
74.0%
Female
Male
Sex

FIGURE 2

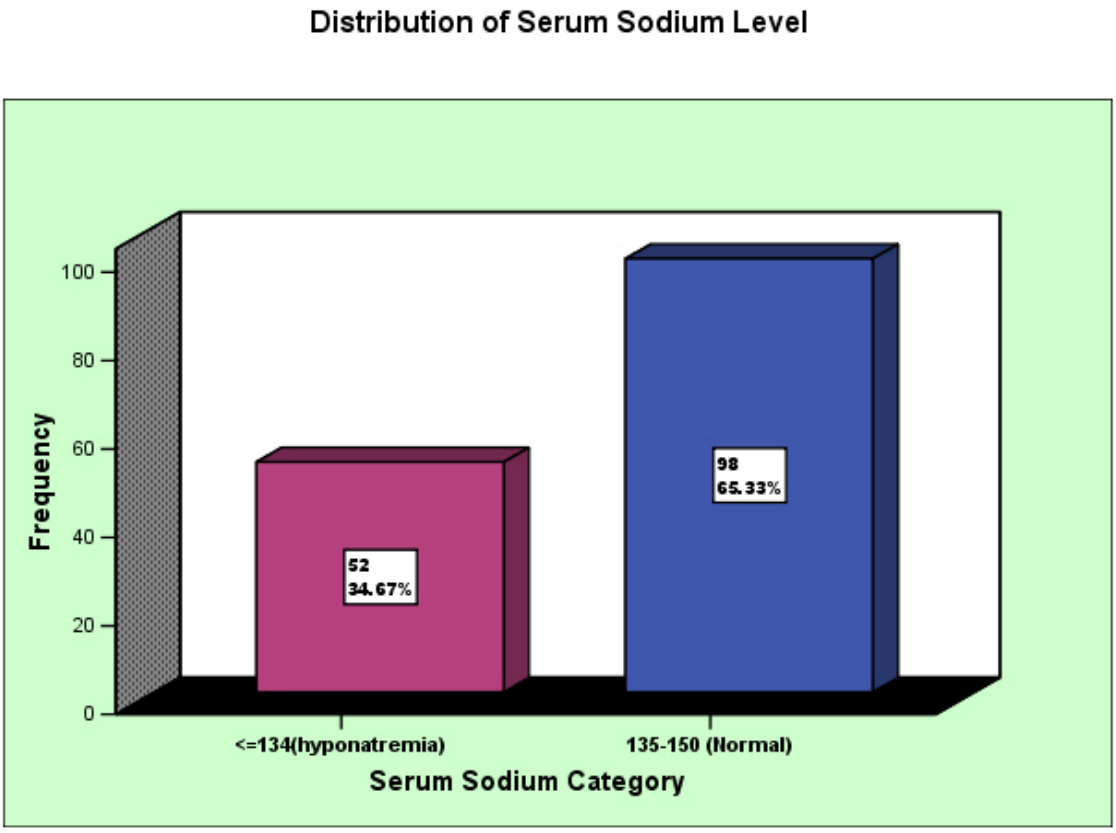

Distribution of Serum Sodium Level
Frequency
100
80
60
40
20
0
52
34.67%
98
65.33%
<=134(hyponatremia)
135-150 (Normal)
Serum Sodium Category

FIGURE 3

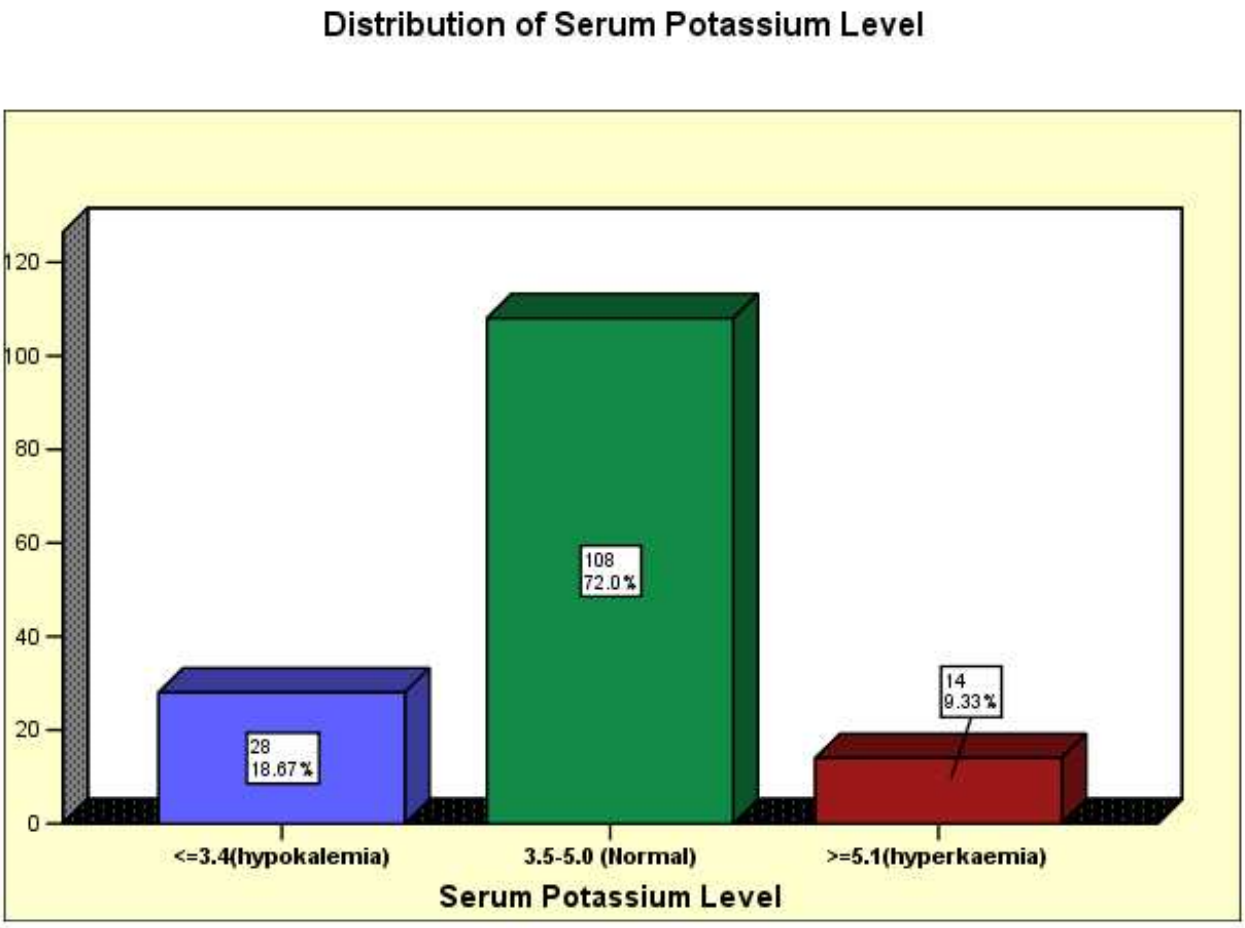

Distribution of Serum Potassium Level
120
100
80
60
40
20
0
28
18.67%
108
72.0%
14
9.33%
<=3.4(hypokalemia)
3.5-5.0 (Normal)
>=5.1(hyperkaemia)
Serum Potassium Level

FIGURE 4) SEX DISTRIBUTUON OF SERUM SODIUM LEVELS

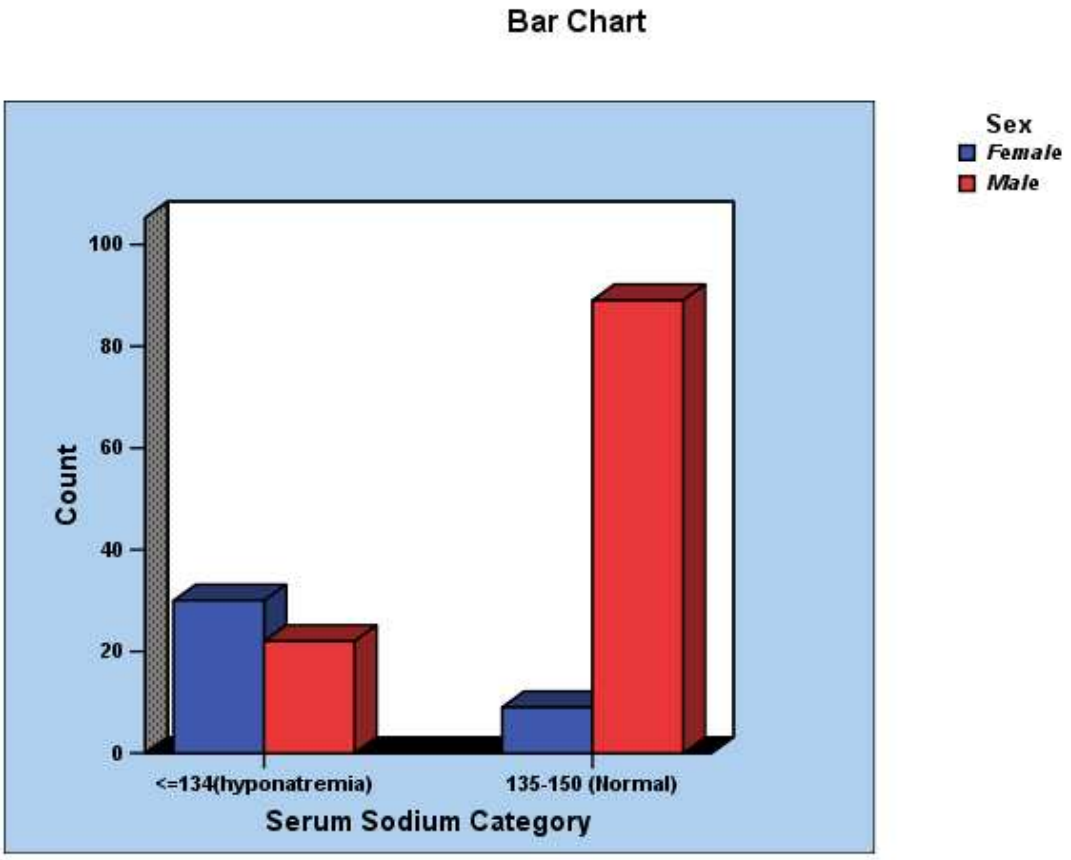


FIGURE 5) SEX DISTRIBUTUON OF SERUM POTASSIUM LEVELS

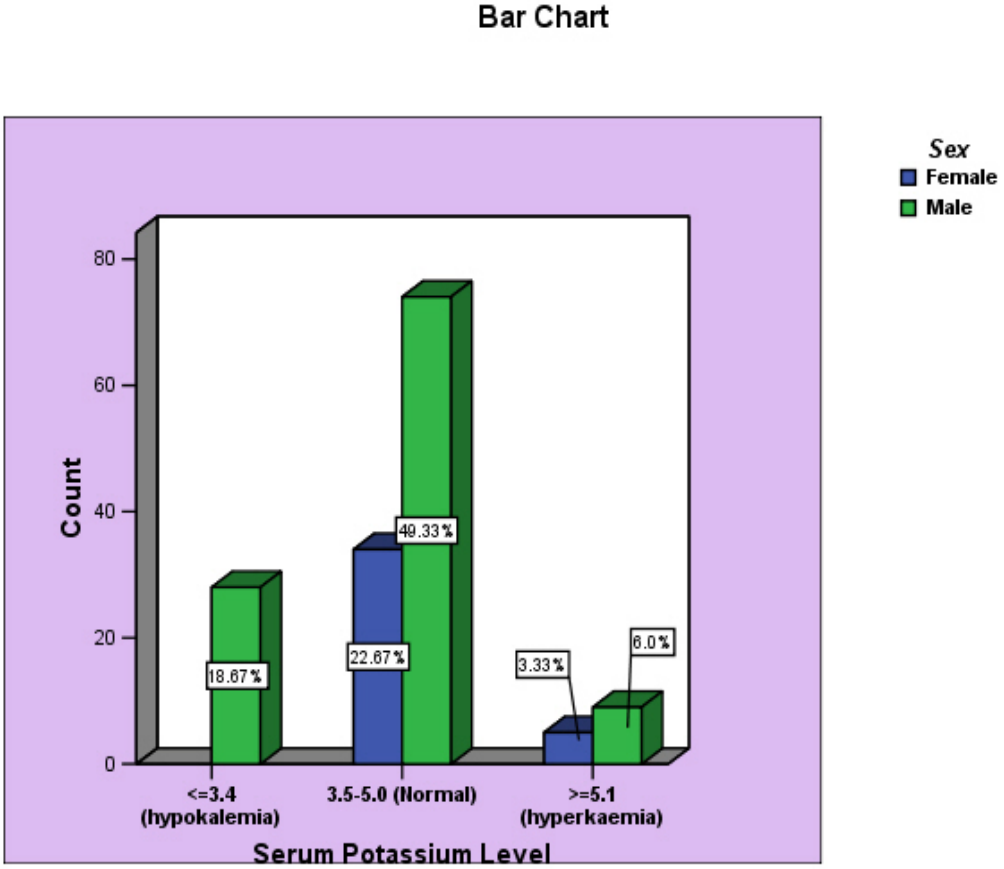


FIGURE 6) FREQUENCY DISTRIBUTUON OF SERUM SODIUM LEVELS

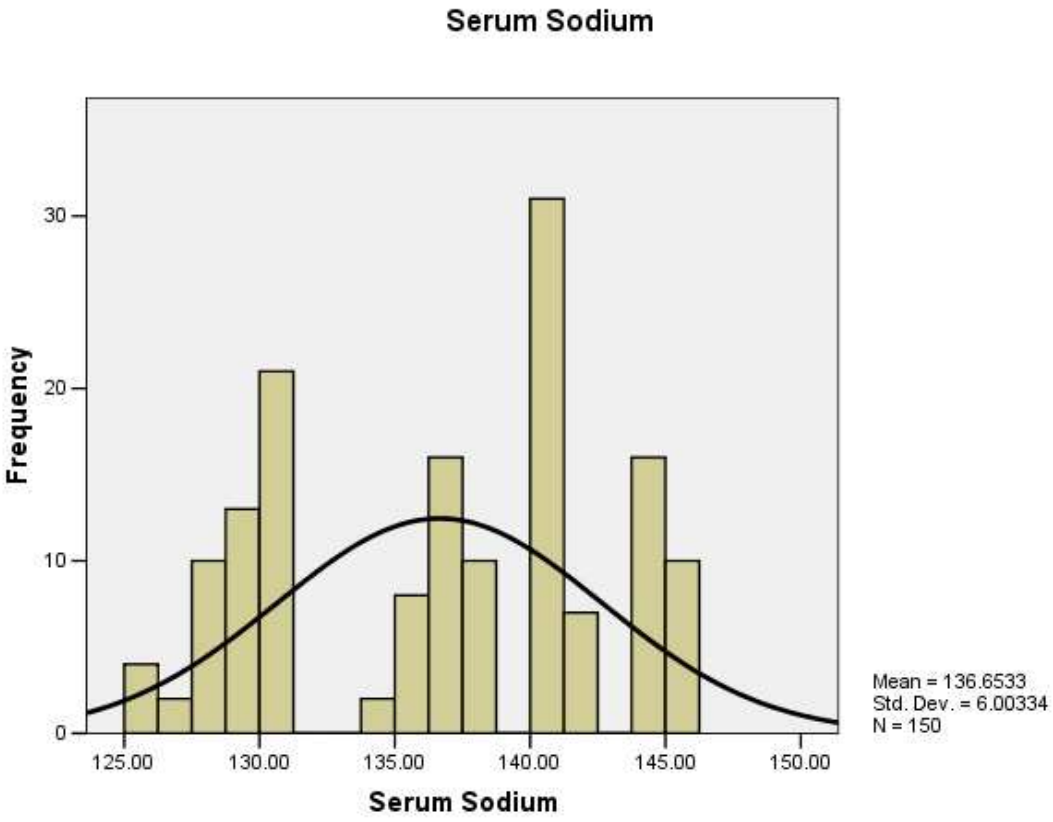
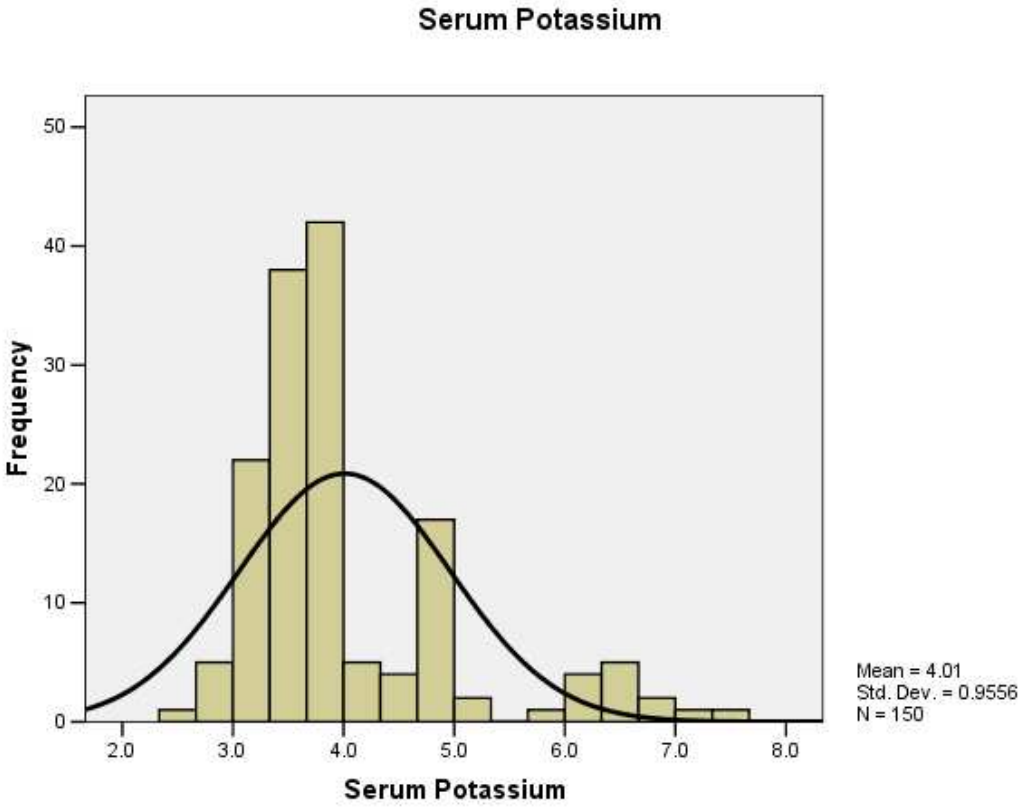


FIGURE 7) FREQUENCY DISTRIBUTUON OF SERUM POTASSIUM LEVELS



RESULTS AND ANALYSIS

The results obtained from this present study as shown in table 2.

TABLE 2

		Age	CD4 count	Blood Sugar	Blood Urea Nitrogen	Creatinine	Serum Sodium	Serum Potassium
N	Valid	150	150	150	150	150	150	150
	Missing	0	0	0	0	0	0	0
Mean		30.85	209.4533	78.2800	16.3943	.99867	136.6533	4.010
Std. Deviation		4.781	80.88019	15.45512	1.83796	.138538	6.00334	.9556
Minimum		24	75.00	60.00	12.67	.600	125.00	2.5
Maximum		39	349.00	100.00	20.00	1.200	146.00	7.4

It indicate the mean age is 30.85 ± 4.78 (±1SD). The minimum and maximum CD4+ counts are 75, 349/micro litre respectively. The mean CD4 count is 209.45±80.88/micro litre (±1SD).The mean serum sodium level is 136.65±6.00(±1SD)Meq/litre. The minimum and maximum serum sodium level are 125 Meq/litre,146 Meq/litre respectively (Figure 6) (Table 1).The mean serum potassium levels is4.01±0.95 Meq/litre (±1SD). The minimum and maximum serum potassium levels observed are 2.5 Meq/litre,7.4 Meq/litre respectively (table 2) (Figure 7).

Among 150 pt's, 52 pt's had hyponatremia and 98 patients had normal sodium levels (Figure2). The percentage of hyponatremia is 34.7%. Among the 52 patients, female patients are 32 and males are 20 . And the percentage of hyponatremia for both males and females are 14.7%, 20.0% respectively (table 3) (Figure 4).

TABLE 3)DISTRIBUTION OF SERUM SODIUM LEVEL

		FREQUENCY	PERCENT
VALID	<=134(HYPONATREMIA)	52	34.7
	135-150 (NORMAL)	98	65.3
	TOTAL	150	100.0

There is a significant correlation between serum sodium levels and CD4+ cell count (Pearson correlation is 0.622). Correlation is significant at the 0.01 level (2-tailed) (table 4).

TABLE 4)CORRELATIONS BETWEEN CD4 COUNT AND SERUM SODIUM LEVEL

		CD4 COUNT	SERUM SODIUM
CD4 COUNT	PEARSON CORRELATION	1	.622(**)
	SIG. (2-TAILED)		.000
	N	150	150
SERUM SODIUM	PEARSON CORRELATION	.622(**)	1
	SIG. (2-TAILED)	.000	
	N	150	150

** CORRELATION IS SIGNIFICANT AT THE 0.01 LEVEL (2-TAILED).

Relationship between Serum Sodium and CD4 Count is shown in table 5.

TABLE NO 5 : RELATIONSHIP BETWEEN SERUM SODIUM AND CD4 COUNT

SERUM SODIUM		N	MEAN	STD. DEVIATION	T TEST (P VALUE)
CD4 COUNT	<=134(HYPONATREMIA)	52	128.5577	40.65320	0.000***
	135-150 (NORMAL)	98	252.3776	61.72395	

Among 150 pt's, 28 pt's had hypokalemia and 108 patients had normal potassium levels, 14 patients had hyper kalemia (Figure 3). The percentage of hypokalemia is 18.7%. the percentage of normal potassium level is 72.0%. The percentage of hyperkalemia is 9.3% (table 6) (Figure 3).

TABLE 6)DISTRIBUTION OF SERUM POTASSIUM LEVEL

		FREQUENCY	PERCENT
VALID	<=3.4(HYPOKALEMIA)	28	18.7
	3.5-5.0 (NORMAL)	108	72.0
	>=5.1(HYPERKAEMIA)	14	9.3
	TOTAL	150	100.0

All patients with Hypokalemia are males (figure 5). Among 108 patients with normal potassium levels female and male patients are 34 , 74 respectively(figure 5), with the percentage of 22.7% and 49.3% respectively. Among 14 patients with hyperkalemia 9 patients are males and 5 patients are females, with the percentage of 6.0% and 3.3% respectively(figure 5).There is no significant correlation between serum potassium levels and CD4+ cell count (Pearson correlation is 0.058) (table 7).

TABLE 7

Correlation Between Serum Potassium And CD4 Count

		CD4 count	Serum Potassium
CD4 count	Pearson Correlation	1	.058
	Sig. (2-tailed)		.479
	N	150	150
Serum Potassium	Pearson Correlation	.058	1
	Sig. (2-tailed)	.479	
	N	150	150

Relationship Between Cd4 Count and Serum Potassium Level By ANOVA is shown in table 8.

TABLE 8) RELATIONSHIP BETWEEN CD4 COUNT AND SERUM POTASSIUM LEVEL BY ANOVA

CD4 COUNT

	SUM OF SQUARES	DF	MEAN SQUARE	**F**	***SIG.***
BETWEEN K+ CATEGORIES	12980.861	2	6490.431	**.992**	***.373***
WITHIN K+ CATEGORIES	961718.312	147	6542.301		
TOTAL	974699.173	149			

DISCUSSION

Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disorders with HIV infected patients. I describe here a high incidence of electrolyte disorders among HIV infected patients admitted in Govt. Rajaji Hospital, Madurai. Numerous factors might have contributed to such high rates of electrolyte disturbances.

Among 150 patients, 52 patients had hyponatremia. The percentage of hypo natremia is 34.7%.

The high incidence of hyponatremia may be due to

1. volume depletion caused by diarrhea or vomiting[18]
2. persistent release of antidiuretic hormone resulting from infections[23]
3. the syndrome of inappropriate antidiuretic hormone (SIADH) [18].

Persistent vomiting, and the the syndrome of inappropriate antidiuretic hormone (SIADH) will cause hypo osmolar hyponatremia. But in SIADH the volume status will be euvolemic[12].

In one study, Burton D Rose et al found that Hyponatremia and hyperkalemia are the two major electrolyte disorders that may be associated with HIV infection[38]. In addition, lactic acidosis, hyperuricemia, and hypophosphatemia have been described[38]. And they have found that the incidence of hyponatremia in hospitalized HIV-infected patients has been reported to be between 35 and 55 percent. The results were comparable to this study.

SIADH in HIV infection may be associated with common pulmonary and intracranial diseases such as Pneumocystis jiroveci pneumonia, toxoplasmosis, and tuberculosis, since most of the patients were admitted for their opportunistic infections.

SIADH is diagnosed by confirming

(a) a hypo-osmotic hyponatremia,

(b) an inappropriately concentrated urine (urine

osmolality >100 mOsm/L),

(c) euvolemia, and

(d) An absence of adrenal, and thyroid dysfunction or other conditions associated with increased ADH action.

Hyponatremia due to volume depletion caused by diarrhea or vomiting can be distinguished from the SIADH by the low urine sodium concentration (usually below 15 meq/L) and correction of the hyponatremia with fluid repletion[38]. Defective renal sodium conservation due to HIV infection of the kidney it self can cause hyponatremia[20].

There is a significant correlation between serum sodium levels and CD4+ cell counts (Pearson correlation is 0.622). Correlation is significant at the 0.01 level (2-tailed) .This is probably because that the opportunistic infections are more common with lower CD4+ cell counts.

Among 150 pt's, 28 pt's had hypokalemia and 108 patients had normal potassium levels, 14 patients had hyper kalemia (Figure 3). The percentage of hypokalemia is 18.7%. The percentage of normal potassium level is 72.0%.The percentage of hyperkalemia is 9.3%. Both hypokalemia and hyperkalemia are common with HIV infection. In this study Hypokalemia(18.7%) more common than hyperkalemia(9.3%). There is no

significant correlation between serum potassium levels and CD4+ cell count (Pearson correlation is 0.058) (table 3).

Hypokalemia may be because of gastrointestinal infections causing vomiting or diarrhea[24,25,26]. Amphotericin B, frequently used to treat fungal infections in patients with AIDS, can cause tubular dysfunction resulting in hypokalemia. Tenofovir has been associated with proximal tubular dysfunction resulting in an electrolyte wasting state, including life-threatening Hypokalemia.[24,25,26]

Drug-induced hyperkalemia is common among patients receiving either high-dose trimethoprim-sulfamethoxazole or intravenous pentamidine[27,28]. In a manner similar to the action of potassium-sparing diuretics such as amiloride, both drugs inhibit distal nephron sodium transport, leading to a decrease in potassium secretion[27,28]. Hyperkalemia and hyponatremia also may be a manifestation of mineralocorticoid deficiency resulting from adrenal insufficiency or the syndrome of hyporeninemic hypoaldosteronism[29,30]. Adrenal causes of hyperkalemia often respond clinically to treatment of the underlying disorder, loop diuretics, or fludrocortisone[30]

This study does have certain limitations, including a limited sample size. The etiology of the electrolyte disturbances were not identified because of limited resources.

CONCLUSION

Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disorders with HIV infected patients. Because of the high incidence of the electrolyte disturbances with HIV infected patients, close monitoring and aggressive management are mandatory.

APPENDIX

ABBREVIATIONS

HIV- HUMAN IMMUNODEFICIENCY VIRUS

AIDS- AQUIRED IMMUNO DEFICIENCY SYNDROME

SIADH- SYNDROME OF INAPPROPRIATE ANTI DIURETIC HARMONE SECRETION

ELISA- ENZYME LINKED IMMUNO SORBANT ASSAY

RT-PCR- REAL TIME POLYMERASE CHAIN REACTION

CD- CLUSTER OF DIFFERENTIATION

HTLV- HUMAN T CELL LYMPHOTROPHIC VIRUS

TALH- THICK ASCENDING LOOP OF HENLE

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Electrolyte disturbances in HIV infected patients Proforma

Name: **Age/sex:**

Ip.No: **Date:**

HIV infection status:

Duration of HIV positivity:

CD4 count: **/microlitre.** **CD4 %:**

H/o ART: Yes/No, If yes duration:

Opportunistic infections: Present/Not present.

If present, details:

Clinical details:

Volume status: hypovolemia/euvolemia/volume overload

Anorexia/nausea/Vomiting/diarrhea/confusion/

head ache/lethargy/convulsion/ coma/muscle cramps/tetany/weakness

H/o any other drug intake: Yes / No,

If yes details:

BP: / mmHg. Pulse: /min. Urine output: ml/day.

Laboratory Data:

Bl.sug: mg/dl. Blood urea nitrogen: mg/dl.

Serum creatinine: mg/dl

Serum Na+: mmol/l. Serum K+: mmol/l.

Sr.Cl-: mmol/l. Sr.HCO3-: mmol/l.

Calculated serum osmolarity: mmol/l.

Spot urine Na: mmol/l.

Calculated urine osmolarity: mmol/l.

Summary:

MASTER CHART

S.No	Age	Sex	CD4 count		Sug	BUN	Creatinine	Sr.Electrolytes	
								Sr.Na+	Sr.K+
1	31	M	160		69	18	1	131	4.8
2	32	M	120		71	17	1.2	131	3.2
3	27	F	75		100	14.08	0.9	125	3.8
4	34	M	240		63	16	1.1	140	4.9
5	32	M	200		98	19	1	144	3.5
6	37	M	310		60	16	1.1	141	4.4
7	26	M	320		70	18.03	1.1	138	3.8
8	31	M	160		69	18	1	131	6
9	27	F	75		100	14.08	0.9	126	3.8
10	35	M	208		63	16	1.1	140	4.9
11	35	M	179		95	15	0.9	146	3.5
12	28	M	349		70	12.67	1.2	142	3.6
13	26	F	80		97	14.08	0.7	128	6.2
14	34	M	240		63	16	1.1	140	4.1
15	39	M	155		66	18	1	131	5
16	37	M	310		60	16	1.1	141	4.9
17	33	M	184		95	18	0.9	146	3.5
18	24	M	290		73	17	1.1	137	6.5
19	37	M	310		60	16	1.1	141	4.4
20	33	M	184		95	18	0.9	146	3.5
21	34	M	240		63	16	1.1	140	4.9
22	30	M	208		98	17	1	144	6.9
23	29	M	320		70	16	1.1	138	3.8
24	28	F	84		97	14.08	0.6	127	3.8
25	24	M	290		73	17	1.1	137	3.8
26	35	M	208		63	16	1.1	140	3.2
27	32	M	120		71	17	1.2	131	3.2
28	26	F	80		97	14.08	0.7	128	3.8
29	39	F	155		66	18	1	131	5
30	33	M	184		95	18	0.9	146	3.5
31	24	M	290		73	17	1.1	137	6.1
32	36	M	164		69	18	1	131	4
33	24	F	175		100	14.08	0.8	129	3.8
34	30	M	208		98	17	1	144	3.5
35	29	M	320		70	16	1.1	138	3.8
36	26	F	80		97	14.08	0.7	128	3.8
37	39	M	155		66	18	1	134	2.9
38	28	F	84		97	14.08	0.6	128	3.8
39	37	M	165		66	18	1	137	3.2
40	37	M	165		66	18	1	137	3.2
41	37	M	320		60	16	1.1	141	4.7
42	32	M	200		98	17	1	144	3.5
43	37	M	320		60	16	1.1	141	4.7
44	37	M	310		60	16	1.1	141	3.2
45	32	M	200		98	17	1	144	3.5

46	24	F	175	100	14.08	0.9	125	3.8
47	35	M	179	95	15	0.9	146	3.5
48	28	M	349	70	12.67	1.2	142	3.6
49	24	M	290	73	20	1.1	137	6.4
50	25	M	209	67	19	1	135	3.6
51	31	M	160	69	18	1	131	3.8
52	27	F	75	100	14.08	0.9	127	7.4
53	32	M	200	98	19	1	144	3.5
54	26	M	320	70	18.03	1.1	138	3.8
55	32	M	200	98	19	1	144	3.5
56	26	M	320	70	18.03	1.1	138	6.9
57	26	F	80	97	14.08	0.7	128	3.8
58	39	M	155	66	18	1	131	2.9
59	33	M	184	95	18	0.9	146	3.5
60	37	M	310	60	16	1.1	141	4.9
61	34	F	240	63	16	1.1	140	4.1
62	24	F	290	73	20	1.1	137	4.8
63	25	M	209	67	19	1	135	3.6
64	25	M	209	67	19	1	135	3.6
65	28	M	349	70	12.67	1.2	142	3.6
66	24	F	175	100	14.08	0.9	129	3.8
67	37	M	310	60	16	1.1	141	3.2
68	32	M	200	98	17	1	144	3.5
69	37	M	310	60	16	1.1	141	3.2
70	28	F	84	97	14.08	0.6	128	3.8
71	24	F	175	100	14.08	0.8	129	5.8
72	30	M	208	98	17	1	144	3.5
73	36	M	164	69	18	1	130	3.2
74	28	M	349	70	12.67	0.9	142	3.6
75	32	M	120	71	17	1.2	131	3.2
76	24	F	175	100	14.08	0.8	129	3.8
77	29	M	320	70	16	1.1	138	3.8
78	25	F	159	81	15.49	1	135	3.5
79	24	F	175	100	14.08	0.9	129	3.8
80	24	M	290	73	17	1.1	137	3.8
81	31	M	160	69	18	1	131	6.4
82	27	F	75	100	14.08	0.9	129	3.8
83	32	M	200	98	19	1	144	3.5
84	35	M	208	63	16	1.1	140	3.2
85	28	M	349	70	12.67	0.9	142	3.6
86	26	F	320	70	18.03	1.1	138	3.8
87	35	M	208	63	16	1.1	140	4.9
88	36	M	164	69	18	1	131	4
89	32	M	120	71	17	1.2	130	3.2
90	37	M	165	66	18	1	137	2.7
91	37	M	320	60	16	1.1	141	3.2
92	24	F	175	100	14.08	0.8	129	3.8
93	29	M	320	70	16	1.1	138	3.8
94	25	F	159	81	15.49	1	135	3.5
95	37	M	165	66	18	1	137	2.7

96	37	M	320	60	16	1.1	141	3.2
97	35	M	179	95	15	0.9	146	3.5
98	24	F	290	73	20	1.1	137	3.8
99	35	M	179	95	15	0.9	146	3.5
100	24	M	290	73	20	1.1	137	3.8
101	36	M	164	69	18	1	131	3.2
102	30	M	208	98	17	1	144	3.5
103	28	F	84	97	14.08	0.6	128	3.8
104	32	M	200	98	17	1	144	3.5
105	37	M	310	60	16	1.1	141	3.2
106	24	F	175	100	14.08	0.9	129	3.8
107	28	M	349	70	12.67	1.2	142	3.6
108	25	M	209	67	19	1	135	3.6
109	31	M	160	69	18	1	131	4.8
110	32	M	120	71	17	1.2	131	3.2
111	27	F	75	100	14.08	0.9	129	3.8
112	34	M	240	63	16	1.1	140	4.9
113	32	M	200	98	19	1	144	3.5
114	37	M	310	60	16	1.1	141	4.4
115	26	M	320	70	18.03	1.1	138	3.8
116	31	M	160	69	18	1	131	3.8
117	27	F	75	100	14.08	0.9	129	6.2
118	35	M	208	63	16	1.1	140	4.9
119	37	F	310	60	16	1.1	141	4.4
120	33	M	184	95	18	0.9	146	3.5
121	34	M	240	63	16	1.1	140	4.9
122	30	M	208	98	17	1	144	6.4
123	29	M	320	70	16	1.1	138	3.8
124	28	F	84	97	14.08	0.6	128	3.8
125	24	M	290	73	17	1.1	137	3.8
126	35	M	208	63	16	1.1	140	3.2
127	32	M	120	71	17	1.2	131	3.2
128	26	F	80	97	14.08	0.7	128	3.8
129	39	M	155	66	18	1	134	2.9
130	28	F	84	97	14.08	0.6	128	3.8
131	37	M	165	66	18	1	137	3.2
132	37	M	165	66	18	1	137	3.2
133	37	M	320	60	16	1.1	141	4.7
134	32	M	200	98	17	1	144	3.5
135	37	M	320	60	16	1.1	141	4.7
136	37	M	310	60	16	1.1	141	3.2
137	32	M	200	98	17	1	144	3.5
138	24	F	175	100	14.08	0.9	129	3.8
139	26	F	80	97	14.08	0.7	126	3.8
140	39	M	155	66	18	1	131	2.5
141	33	F	184	95	18	0.9	146	3.5
142	37	M	310	60	16	1.1	141	4.9
143	34	M	240	63	16	1.1	140	4.1
143	24	M	290	73	20	1.1	137	3.8
145	25	F	209	67	19	1	135	7

146	25	M	209	67	19	1	135	3.6
147	28	M	349	70	12.67	1.2	142	3.6
148	24	F	175	100	14.08	0.9	129	3.8
149	31	M	160	69	18	1	131	3.8
150	27	F	75	100	14.08	0.9	129	6.2