Section: General Medicine

Original Research Article

A STUDY OF ELECTROLYTE DISTURBANCES IN HIV INFECTED PATIENTS AND IT'S CORRELATION WITH CD4 COUNT

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ABSTRACT

Background: Acquired Immunodeficiency Syndrome (AIDS) is a disease caused by a retrovirus Human Immunodeficiency Virus (HIV). It is characterized by marked immunosuppression which results in opportunistic infections, secondary neoplasms and neurologic manifestations. **Objective:** Identification of electrolyte disturbances among HIV infected patients and correlation with CD4 counts.

Material and Methods: This Prospective cross-sectional study includes all 100 patients infected with HIV Admitted in medicine wards, Al- Ameen Medical College, Athani Road, Vijayapur during a period from November 2018 to May 2020. Both male and female patients were included in this study.

Results: The percentage of hyponatremia is 42%. Percentage of hyponatremia for both males and females are 50% each. There is a significant correlation between serum sodium levels and CD4+ cell counts (Pearson correlation is 0.627). Correlation is significant at the p value <0.001 level. Both hypokalemia and hyperkalemia are common with HIV infection. In this study Hypokalemia (21%) more common than hyperkalemia (9%). There is no significant correlation between serum potassium levels and CD4+ cell count (Pearson correlation is 0.094 and p value is 0.355). Hyponatremia is a marker of the severity of HIV- disease but not an independent risk factor for mortality. Hyponatremic HIV patients had a lower CD4 cell Count, a higher prevalence of AIDS and were more frequently hospitalized at first contact compared to normonatremic patients.

Conclusion: Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disorders with HIV infected patients. Lower the CD4 Count, higher the risk of opportunistic infections and higher incidence of electrolyte disturbances. Hyponatremia is the most frequent electrolyte abnormality in HIV/AIDS patients. Severe hyponatremia, unlike other electrolyte disorder, is associated with a lower CD4 Count.

Keywords: AIDS, HIV, Electrolyte Disturbances

INTRODUCTION

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 immunodeficiencyvirus/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.[1]

HIV continues to be a major global public health issue, having claimed almost 33 million lives so far. However, with increasing access to effective HIV prevention, diagnosis, treatment and care, including for opportunistic infections, HIV infection has become a manageable chronic health condition, enabling people living with HIV to lead long and healthy lives.[2]

There were an estimated 38.0 million people living with HIV globally at the end of 2019. In 2019, 68% of adults and 53% of children living with HIV globally were receiving lifelong antiretroviral therapy (ART).

A great majority (85%) of pregnant and breastfeeding women living with HIV also received ART, which not only protects their health, but also ensures prevention of HIV transmission to their newborns. However, not everyone is able to access HIV testing, treatment and care. Notably, the 2018 Super-Fast-Track targets for reducing new paediatric HIV infections to 40,000 was not achieved. Global targets for 2020 areat risk of being missed unless rapid action is taken. Due to gaps in HIV services, 6,90,000 people died from HIV-related causes in 2019 and 1.7 million people were newly infected.[2]

Key population groups and their sexual partners accounted for over 60% of all new HIV infections globally among the age group 15-49 years (an estimated 62%) in 2019. In eastern European and central Asia, Asia and the Pacific, western and central Europe and north America and Middle East and north Africa, these groups accounted for over 95% of new HIV infections in each of these regions.

WHO defines key populations as people in populations who are at increased HIV risk in all countries and regions. Key populations include: men who have sex with men; people who inject drugs; people in prisons and other closed settings; sex workers and their clients; and transgender people.

At the end of 2019, an estimated 81% of people living with HIV knew their status. 67% were receiving antiretroviral therapy (ART) and 59% had achieved suppression of the HIV virus with no risk of infecting others. At the end of 2019, 25.4 million people were accessing antiretroviral therapy. Between 2000 and 2019, new HIV infections fell by 39% and HIV-related deaths fell by 51%, with 15.3 million lives saved due to ART. This achievement was the result of great efforts by national HIV programmes supported by civil society and international development partners.[2]

Patients with advanced HIV disease may develop hyponatremia due to syndrome of inappropriate antidiuretic hormone secretion (SIADH) as a consequence of increased free water intake and decreased free water excretion. SIADH is usually seen in conjunction with pulmonary or CNS disease3. Volume depletion due to diarrhoea and vomiting is the usual cause of hyponatremia. Low serum sodium may also be due to adrenal insufficiency; a concomitant high serum potassium is seen.

Hyperkalemia may be secondary to adrenal insufficiency; HIV nephropathy; or medications, particularly trimethoprim and pentamidine.

Hypokalemia is seen with tenofovir or amphotericin therapy. Hypokalemia is predictably seen secondary to gastrointestinal losses of potassium in HIV patients with gastrointestinal infections. Adrenal gland disease may be due to mycobacterial infections, CMV disease, cryptococcal disease, histoplasmosis or ketoconazole toxicity.

ART is cornerstone of ever- evolving clinical management scheme of patients with HIV infection and AIDS. Both HIV infection and ART lead to adverse physiological changes, which are predisposing factors for electrolyte complications.[4]

Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disorders with HIV infected patients. Because of high incidence of electrolyte disturbances with HIV infected patients, close monitoring and aggressive management are mandatory.[5] Hence present study aims at identification of electrolyte disturbances among HIV infected patients and correlation with CD4 counts.

MATERIALS AND METHODS

100 patients admitted with HIV infection in the medicalwards, AL- Ameen Medical College, Vijayapur from November 2018 to May 2020 forms the study group.

Inclusion Criteria

- All patients with HIV infection, admitted in medicine wards were included in this study.
- Only symptomatic patients and patients with opportunistic infections(eg. T.B meningitis, chronic diarrhea, etc) were included in this study.

Exclusion Criteria

- Asymptomatic patients were not included in this study.
- Impaired renal function itself can alter the serum electrolytes, patients with elevated renal parameters were not included in this study.
- Patients with hyperglycemia and hyperlipidemia were excluded from this study.

Sample Size Calculation

With 95% confidence level and margin of error of ±10%, a sample size of 97 (≈100) subjects will allow the study to determine the Electrolyte Disturbances in HIV Infected Patients and It's correlation with CD4 Count

Total sample size= 100

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate of Electrolyte Disturbances

Ethical Consideration

Informed written consent was taken from all enrolled patients after detailed counseling. The contents of the consent was taken in patient's own language.

Procedure of Study and Equipment

- All 100 patients were tested for HIV-1 .
- Test was repeated and confirmed for all patients. WESTERN BLOT could not be performed because of limited resources.
- Tests for CD4+ count, Blood sugar, Lipid profile, Blood urea, Serum creatinine, Serum sodium, Serum potassium were done for all patients and 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 were done.
- BUN (Blood Urea Nitrogen) values were calculated by using formula (BUN=blood urea/2.13).

Statistical Analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F test of testing of equality of Variance.

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23 (IBM Statistics, Chicago, USA) and Microsoft office 2007.

RESULTS

During the study period 100 HIV infected patients were tested for CD4 Count, Blood sugar, Lipid profile, Blood Urea, Serum Creatinine, Serum Sodium and Serum Potassium.

Highest number of HIV infected patients were in the age group 31-35years, followed by patients between 26-30 years. The mean age of HIV infected patients is 30.7 ±4.8 (±1SD).

There were 75 males (75%) and 25 females (25%) among the total number of HIV infected patients. [Table 1]

Among 100 patients, 42 patients had hyponatremia and 58 patients had normal sodium levels. [Table 2]

Among 100 pt's, 21 pt's had hypokalemia and 70 patients had normal potassium levels, 9 patients had hyperkalemia. The percentage of hypokalemia is 21%. The percentage of normal potassium level is 70%. The percentage of hyperkalemia is 9%. [Table 3]

The minimum and maximum CD4 counts are 75 and 349/micro litre respectively.

The mean CD4 Count is 210.6 ±82.4/micro litre (±1SD). The mean serum sodium is 135.9±6.2 (±1SD) Meq/litre.

The minimum and maximum serum sodium levels are 124 and 146 Meq/litre respectively. The mean serum potassium levels is 4±1Meq/litre(±1SD).

The minimum and maximum serum potassium levels are 2.7 and 7.4 Meq/litre respectively.

There is significant correlation between serum sodium levels and CD4 Count (Pearson correlation is 0.627). [Table 4]

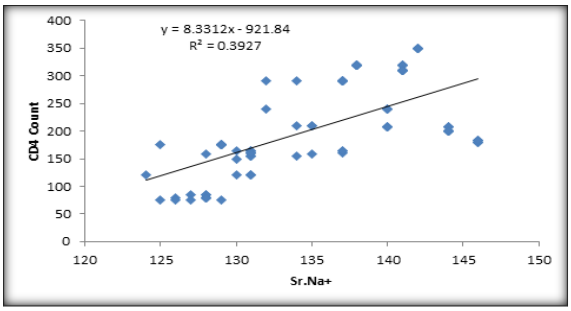

Figure 1: Correlation of CD4 Count with Sr.Na+

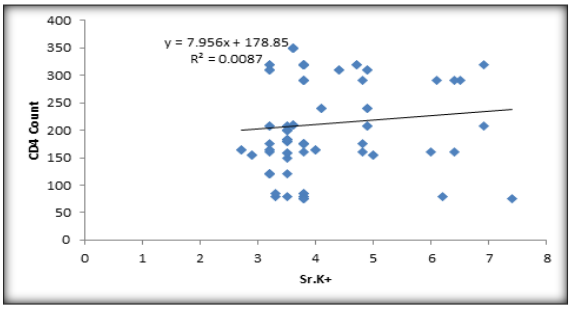

Figure 2: Correlation of CD4 Count with Sr.K+

There is no significant correlation between serum potassium levels and CD4+ cell count (Pearson correlation is 0.094 and p value is 0.355). [Table 6]

The percentage of hyponatremia is 42%. Among 42 patients, female patients are 21 and male patients are 21 and the percentage of hyponatremia for both males and females are 50% each. [Table 8]

Among 21 patients of hypokalemia, 18 are male and 3 are female with the percentage of 85.7% and 14.3% respectively. Among 70 patients with normal potassium levels male and female patients are 50, 20 respectively, with the percentage of 71.4% and 28.6% respectively.

Among 9 patients with hyperkalemia 7 patients are males and 2 patients are females, with the percentage of 77.8% and 22.2% respectively. [Table 10]

Table 1: Association of Age and Sex

Age (yrs)	Male		Female		p value
	N	%	N	%	
21-25	9	12.0%	11	44.0%	<0.001*
26-30	15	20.0%	12	48.0%	
31-35	30	40.0%	1	4.0%	
36-40	21	28.0%	1	4.0%	
Total	75	100.0%	25	100.0%	

Note: * significant at 5% level of significance (p<0.05)

Table 2: Distribution of Cases according to Sr.Na+

Sr.Na+	N	%
Hyponatremia(≤134)	42	42
Normal(135-150)	58	58
Total	100	100

Table 3: Distribution of Cases according to Sr.K+

Sr.K+	N	%
Hypokalemia≤3.4)	21	21
Normal(3.5-5.0)	70	70
Hyperkalemia(>5.0)	9	9
Total	100	100

Table 4: Descriptive Statistics of Study parameters

Descriptive Statistics	Min	Max	Mean	SD
CD4 Count	75	349	210.6	82.4
RBS	60	100	78.4	15.2
BUN	12.67	20	16.4	1.9
Creatinine	0.6	1.2	1.0	0.1
Sr.Na+	124	146	135.9	6.2
Sr.K+	2.7	7.4	4.0	1.0

Table 5: Mean CD4 Count according to Sr.Na+

CD4 Count	Hyponatremia(≤134)		Normal(135-150)		p value
	Mean	SD	Mean	SD	
	143.6	54.0	259.2	63.1	<0.001*

Table 6: Mean CD4 Count according to Sr.K+

CD4 Count	Hypokalemia(≤3.4)		Normal(3.5-5.0)		Hyperkalemia(>5.0)		p value
	Mean	SD	Mean	SD	Mean	SD	
	187.3	79.5	217.9	81.6	208.1	94.5	0.330

Table 7: Distribution of Age according to Sr.Na+

Age(yrs)	Hyponatremia(≤134)		Normal(135-150)		p value
	N	%	N	%	
21-25	11	26.2%	9	15.5%	0.608
26-30	11	26.2%	16	27.6%	
31-35	12	28.6%	19	32.8%	
36-40	8	19.0%	14	24.1%	
Total	42	100.0%	58	100.0%	

Table 8: Distribution of Sex according to Sr. Na+

Sex	Hyponatremia(≤134)		Normal(135-150)		p value
	N	%	N	%	
Male	21	50.0%	54	93.1%	<0.001*
Female	21	50.0%	4	6.9%	
Total	42	100.0%	58	100.0%	

Note: * significant at 5% level of significance (p<0.05)

Table 9: Distribution of Age according to Sr. K+

Age (yrs)	Hypokalemia (≤3.4)		Normal(3.5-5.0)		Hyperkalemia (>5.0)		p value
	N	%	N	%	N	%	
21-25	1	4.8%	16	22.9%	3	33.3%	0.001*
26-30	2	9.5%	21	30.0%	4	44.4%	
31-35	6	28.6%	23	32.9%	2	22.2%	
36-40	12	57.1%	10	14.3%	0	0.0%	
Total	21	100.0%	70	100.0%	9	100.0%	

Table 10: Distribution of Sex according to Sr.K+

Sex	Hypokalemia (≤3.4)		Normal (3.5-5.0)		Hyperkalemia (>5.0)		p value
	N	%	N	%	N	%	
Male	18	85.7%	50	71.4%	7	77.8%	0.407
Female	3	14.3%	20	28.6%	2	22.2%	
Total	21	100.0%	70	100.0%	9	100.0%	

DISCUSSION

Hyponatremia, hypokalemia and hyperkalemia are common electrolyte disorders with HIV infected patients. I describe here a high incidence of electrolyte disturbances among HIV infected patients admitted in Al-Ameen Medical College Hospital, Vijayapur. Numerous factors might have contributed to such high rates of electrolyte disturbances.

Among 100 patients, 42 patients had hyponatremia. The percentage of hyponatremia is 42%.

The high incidence of hyponatremia may be due to

1. Volume depletion caused by diarrhea or vomiting.[6]
2. Adrenal insufficiency and hypopituitarism associated with HIV.[7]
3. The syndrome of inappropriate antidiuretic hormone (SIADH).[6]

Persistent vomiting, and the the syndrome of inappropriate antidiuretic hormone (SIADH) will cause hypoosmolar hyponatremia. But in SIADH the volume status will be euvolemic.[8]

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.

Study conducted by Richard H Sterns concludes, Hyponatremia and hyperkalemia are the two major electrolyte disorders that may be associated with HIV infection.[9] In addition, lactic acidosis, hyperuricemia, and hypophosphatemia have been described9. 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.

Study conducted by Braconnier P et al (2017) shows that hyponatremia is a marker of the severity of HIV- disease but not an independent risk factor for mortality as suggested by previous publications. Hyponatremic HIV patients had a lower CD4 cell Count, a higher prevalence of AIDS and were more frequently hospitalized at first contact compared to normonatremic patients.[10]

Hyponatremia is the most frequent electrolyte abnormality in HIV/AIDS patients. Severe hyponatremia, unlike other electrolyte disorder, is associated with a lower CD4 Count. This may be the plausible reason behind association of hyponatremia with higher morbidity and mortality in HIV patients.[11]

Study conducted by Xu L et al (2014) shows frequency of hyponatremia was approximately 53.2% in HIV/AIDS patients. The study revealed a significantly positive correlation between serum sodium concentrations and the number of CD4+ cells and a negative correlation with the WHO clinical stage. These observations indicate that serum sodium concentrations can be used as an indicator of the progression of HIV/AIDS independent of the CD4 count and WHO clinical stage.[12]

There is a significant correlation between serum sodium levels and CD4+ cell counts (Pearson correlation is 0.627) (Table8). Correlation is significant at the p value <0.001 level (Table 9).This is probably because that the opportunistic infections are more common with lower CD4+ cell counts.

Among 100 pt's, 21 pt's had hypokalemia and 70 patients had normal potassium levels, 9 patients had hyperkalemia (Table 6). The percentage of hypokalemia is 21%. The percentage of normal potassium level is 70%. The percentage of hyperkalemia is 9%. Both hypokalemia and hyperkalemia are common with HIV infection. In this study Hypokalemia (21%) more common than hyperkalemia (9%).

Hypokalemia may be because of gastrointestinal infections causing vomiting or diarrhea.[13] 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 lifethreatening Hypokalemia.[14]

Drug-induced hyperkalemia is common among patients receiving either high-dose trimethoprim-sulfamethoxazole or intravenous pentamidine.[15] 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.[16] Hyperkalemia and hyponatremia also may be a manifestation of mineralocorticoid deficiency resulting from adrenal insufficiency or the syndrome of hyporeninemic hypoaldosteronism.[17] Adrenal causes of hyperkalemia often respond clinically to treatment of the underlying disorder, loop diuretics, or fludrocortisones.[18]

There is no significant correlation between serum potassium levels and CD4+ cell count (Pearson correlation is 0.094 and p value is 0.355).

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. Lower the CD4 Count, higher the risk of opportunistic infections and higher incidence of electrolyte disturbances. Hyponatremia is the most frequent electrolyte abnormality in HIV/AIDS patients. Severe hyponatremia, unlike other electrolyte disorder, is associated with a lower CD4 Count. This may be the reason behind association of hyponatremia with higher morbidity and mortality in HIV patients. Because of the high incidence of the electrolyte disturbances among HIV/AIDS patients which results in higher morbidity and mortality. Hence close monitoring, earlier and intensive management is necessary to improve the outcome of such patients.

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