

A Study of Clinical and Biochemical Profile of Adrenal Insufficiency in AIDS Patients.

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ABSTRACT

Most common and clinically relevant endocrine organ dysfunction in AIDS patients is that of adrenal cortex. But, adrenal insufficiency (AI) is seldom diagnosed in clinical practice because symptoms do not appear until more than 90% of the gland has been destroyed and symptoms suggestive of adrenal insufficiency are not uncommon in patients of AIDS without AI. There is lack of studies to look for characteristic features in such group, which can raise a suspicion and lead us to do biochemical evaluation, to detect early HPA axis involvement, to prolong as well as improve quality of life. Fifty HIV seropositive patients were selected, detailed history, clinical examination and biochemical parameters were recorded. Their basal cortisol and 30-min, 60-min, post synacthen test were performed, based on which the patients were grouped as AIDS with AI (AIDS-Ab) and AIDS without AI (AIDS-N). The clinical feature and laboratory findings of these two groups were compared and interpreted using Chi square test as a test of significance and for comparison of laboratory data the Mann Whitney was used. In our study, in comparison to AIDS-N, AIDS-Ab patients had more frequency of weakness, weight loss, fever, gastrointestinal disturbances like nausea, vomiting. They also had lower range of CD4 count, hypoglycemia, high ESR, eosinophilia, hyponatremia, hyperkalemia, low Na/K ratio. In AIDS patients, symptoms like significant weight loss, low CD4 count, not on ART, hypoglycemia, increased ESR, hyponatremia, hyperkalemia, low Na/K ratio, low basal plasma cortisol levels as seen in the present study, should direct us in suspecting the risk of patient going for AI. In such patients stimulation tests could be done to confirm AI. The importance of early detection becomes clear from the fact that AI adds to the mortality of AIDS patient, and also early intervention in such patients prolongs as well as adds quality to life.

INTRODUCTION

The AIDS wasting syndrome is a devastating complication of HIV virus disease characterized by weight loss and inanition ^[1], affecting both homosexual and heterosexual individuals ^[2]. Being a multisystem disease, the endocrine dysfunction results primarily from involvement of the endocrine glands or central nervous system by infectious agents, side effects of drugs and from the wasting suffered by AIDS patients ^[3].

Most common and clinically relevant endocrine organ dysfunction is that of adrenal cortex. The incidence rate is 5%-10%, higher than the incidence in general population ^[4,5]. In developing country it is 0.8 cases in 1 lakh population ^[6]. Adrenal gland involvement has been documented in as many as 2/3rd of patients with AIDS ^[7] and up to 30% in pituitary ^[8] at post mortem examination ^[7]. However, adrenal insufficiency is seldom diagnosed in clinical practice because symptoms do not appear until more than 90% of the gland has been destroyed ^[7]. In

agreement to this only 3% of the patients had an ante mortem diagnosis of adrenal insufficiency among those showing adrenal involvement at post mortem examination [7].

This is because symptoms suggestive of adrenal insufficiency such as weakness, weight loss, hyponatremia and hyperkalemia are not uncommon in patients at advanced stage of HIV infection without adrenal insufficiency, because of concurrent opportunistic diseases and treatment [5]. Infection with HIV, with disturbances of HPA axis, occur both in early and later stages of the disease [6]. The sub-clinical alterations in adreno-cortical functions are described in 0-25% of patients with HIV infection [9]. This subclinical abnormalities may progress to clinically significant AI as the HIV therapies improve and patients with AIDS live longer [10]. Adrenal insufficiency itself increases the mortality rate in HIV patients, but early intervention improves the quality of life and also prolongs life.

But, subjecting all the AIDS patients to laboratory evaluation, to look for AI is practically not feasible. Hence, it is important know the characteristic features in such group, which can raise a suspicion and lead us to laboratory evaluation, to detect early HPA axis involvement.

The aim of the present study was to look for the characteristic clinical and biochemical profile that can aid in diagnosing AI in AIDS patients.

MATERIALS AND METHODS

Fifty HIV seropositive adult men and women over 18 yrs of age, who fulfilled the AIDS defining CDC 1993 criteria [11], those not on drugs known to alter HPA Axis function, those not on corticosteroids in past three months, those with no history of HPA insufficiency/autoimmune disease were selected for the study, with their consent. Ethical clearance was obtained from the ethical clearance committee of the institute.

Study protocol

All the patients of the study were subjected to

Clinical history

Emphasizing on symptoms, history of opportunistic infection, treatment details like ART, corticosteroids, other drugs affecting HPA axis.

Physical examination

Recording of weight, vital signs, muscle mass, pigmentation, blood pressure variation to posture.

Laboratory parameters

Included CD4 count, CBC, ESR, Sr.electrolytes, Random blood sugars

ACTH stimulation test

The intravenous (I.V) catheter was inserted between 7 - 8 am. After taking blood for basal plasma cortisol, 1µg ACTH was given I.V. From the indwelling I.V catheter, the sample was again collected at 30 and 60 minutes after ACTH injection, for plasma cortisol estimation by solid-phase radio-immunoassay.

The value of plasma cortisol of < 18µg/dl, 30 or 60- minutes after the 1µg ACTH test, was considered as indicative of AI.

Statistical Analysis

Clinical features of AIDS patients with AI, was compared with those without AI by Chi square test as a test of significance. For comparison of laboratory data the Mann Whitney was used. The 'P' value of <0.05 was taken as significant.

RESULTS

Out of 50 patients who were included in the study, Synacthen test was found to be positive in 32 patients confirming the presence of adrenal insufficiency and 18 were found to be negative. The patients with +ve results were designated as AIDS-Ab and those with -ve results as AIDS-N. The detailed discussion of the results obtained in the study is described in following tables.

On ART (Anti-Retro viral Therapy) (Table 1):

30 patients out of 37 who were not on treatment.

Symptomatology (Table 2)

AIDS-Ab patients predominantly had weakness, nausea, vomiting, fever and weight loss when compared to AIDS-N group who had fatigue, anorexia, muscle pain and joint pain.

Opportunistic infections (Table 3)

In the present study it was seen that AIDS patients with opportunistic infections had more frequency of adrenal insufficiency. The most common being, PCP.

CD4 count (Table 4)

The CD4 count being higher in AIDS-N shows significant difference from that of AIDS-Ab. Test association for the AIDS patients with AI and lower range of CD4 count also shows significance.

RBS, ESR, Eosinophilia (Table 5)

There was statistically significant hypoglycemia, high ESR and eosinophilia in AIDS-Ab group when compared to AIDS-N group.

Electrolyte composition (Table 5)

There was significant hyponatremia, hyperkalemia, and low Na/K⁺ ratio in AIDS-Ab group in comparison to AIDS-N group.

BP (Table 5)

In our study, both the groups AIDS-N and AIDS-Ab showed no orthostatic hypotension

Basal plasma cortisol (Table 5)

There was statistically significant difference in the basal plasma cortisol of AIDS-N and AIDS-Ab patients.

Synacthen test (Table 5)

Stimulated serum cortisol levels of AIDS-Ab at 30-minute (11.20) and 60-minutes (10.27) were significantly lower than the ones in AIDS-N at 30 minutes (21.06) and 60 minutes (20.03).

Table 1: Comparison of clinical profile of AIDS patients without AI(AIDS-N) and with AI(AIDS-Ab)

Parameters		AIDS-N (n=18)	AIDS-Ab (n=32)	P value
Age(yrs)	Mean ± SD	38.15 ± 5.82	37.75 ± 8.69	0.87(NS)
Gender	Male	12	30	0.15(NS)
	Female	6	2	
Anthropometric Measures	Height(cms)	160.84 ± 11.23	163.54 ± 7.73	0.34(NS)
	weight(Kgs)	46.53 ± 11.46	52.59 ± 10.07	0.07(NS)
	BMI	18.55 ± 3.38	19.58 ± 3.04	0.3(NS)
CDC Classification	A3	3	4	2.7(NS)
	B3	3	4	
	C1	2	0	
	C2	1	2	
ART	C3	9	22	0.04(S)
	Patient's on ART (n=13)	11	2	
	Patient's not on ART (n=37)	7	30	

S- Significant, NS- Non Significant, n- Number of patients

Table 2. Comparison of symptoms between patients of AIDS without Adrenal Insufficiency (AIDS-N) and with Adrenal Insufficiency (AIDS-Ab).

Parameters		AIDS-N (n=18)	AIDS-Ab (n=32)
Symptomatology	Weakness	13	32
	Fatigue	5	20
	Anorexia	4	13
	Nausea	7	16
	Vomiting	4	5
	Fever	4	9
	Weight loss	4	6
	Muscle Pain	0	3
	Joint Pain	0	0
	Hyperpigmentation	0	4
	Diarrhoea	2	2
	Lethargy	5	10

n- Number of patients

Table 3: Comparison of opportunistic infections between patients of AIDS without Adrenal Insufficiency (AIDS-N) and with Adrenal Insufficiency (AIDS -Ab).

Parameters		AIDS-N (n=18)	AIDS-Ab (n=32)
Opportunistic Infections	PCP	3	11
	TB	5	11
	Oral Candidiasis	3	6
	Cryptococcosis	1	3
	Cryptosporidiosis	1	3
	CMV	1	2
	Molluscum	0	1
	Herpes Infection	0	2

n- Number of patients

Table 4: Statistical comparison of CD4 count between patients of AIDS without Adrenal Insufficiency(AIDS-N) and with Adrenal Insufficiency(AIDS-Ab).

Parameters		AIDS-N (n=18)	AIDS-Ab (n=32)	P value
CD4 count(cells/microltr)	Mean	171.8 ± 25.41	138.7 ± 56.17	0.04(S)
	Range			
	0-49	1	4	
	50-99	2	2	
	100-149	2	10	0.028(S)
	150-199	12	12	
	200-249	1	4	

S- Significant, NS- Non Significant, n- Number of patients

Table 5. Comparison of biochemical profile and Blood Pressure (BP) between patients of AIDS without Adrenal Insufficiency (AIDS-N) and with Adrenal Insufficiency (AIDS-Ab).

Parameters		AIDS-N (n=18)	AIDS-Ab (n=32)	P value
RBS(gms%)		124.86 ± 23.07	98.35 ± 19.39	0.00(S)
ESR		49.85 ± 14.51	79.97 ± 34.33	0.004(S)
Eosinophils (cells/cumm)		1.38 ± 1.44	4.5 ± 3.88	0.001(S)
Electrolyte composition	Na+	135.15 ± 4.91	130.97 ± 3.46	0.003(S)
	K+	3.75 ± 0.59	4.37 ± 0.59	0.001(S)
	Na+/K+	35.62 ± 4.7	31.62 ± 4.7	0.003(S)
BP(mmHg)	Standing	115/72	112/72	
	Supine	123/76	122/75	
Serum Cortisol levels (µg/dl)	Basal	24 ± 8.77	11.15 ± 6.06	0.000(S)
	30-min	21.06 ± 1.6	11.20 ± 5.16	0.000(S)
	60-min	20.03 ± 3.91	10.27 ± 5.91	0.000(S)

S- Significant, NS- Non Significant, n- Number of patients

DISCUSSION

Out of 50 AIDS patients selected for the present study, prevalence of adrenal insufficiency among AIDS patients was 64%.

Adrenal insufficiency (AI) is a well-known complication of AIDS. However, the clinical and biochemical features of AI in HIV infected patients have not been extensively studied. The present study showed no statistically significant difference in age, gender preponderance, anthropometric measures and CDC class distribution between AIDS patients with AI (AIDS-Ab) and without AI(AIDS-N).

In the present study, in comparison to AIDS-N, AIDS-Ab patients had more frequency of weakness, weight loss, fever, gastrointestinal disturbances like nausea and vomiting. They also had lower range of CD4 count, hypoglycemia, high ESR, eosinophilia, hyponatremia, hyperkalemia, low Na/K ratio. Other studies have shown weakness [2,12,14], weight loss [4,10,13,14], anorexia [2,10], nausea [2,4,10], hyponatremia [2,10,13,14,15], hyperkalemia [2,10], fatigue [2,14], vomiting [2,4,14], hypotension [12,13,14,15], diarrhea [12,13], hyperpigmentation [12], hyperglycemia [13], mucocutaneous melanosis [14] among the AIDS patients having AI. One study has documented that CD4 count does not predict the presence or absence of AI in AIDS patients¹⁶ contrary to the results in the present study. There was no study available documenting the association between ART and incidence of AI in AIDS patients, as seen in the present study.

In the present study, comparison to AIDS-N, AIDS-Ab patients have shown significantly lower basal cortisol levels, 30-min and 60-min post-synacthen test. Other studies with similar results are, one has documented lower basal cortisol with abnormal response to stimulation test⁴, and in another study, out of 75% of patients with lower basal cortisol levels, and only 2% of them had normal response to synacthen test¹⁷.

Thus lack of references of detailed study of such group of patients emphasizes, need for further studies on larger study sample.

CONCLUSION

The adrenal cortex is a common site of pathological involvement in patients infected with Human Immunodeficiency Virus and AIDS that result from it. In AIDS patients findings like significant weight loss, weakness, fever, GI disturbances, low CD4 count, those patients who are not on ART, patients having hypoglycemia, increased ESR, hyponatremia, hyperkalemia, low Na/K ratio, low basal plasma cortisol levels as seen in the present study, should direct us in suspecting the risk of patient going for AI. In such patients stimulation tests should be done to confirm AI. The importance of early detection becomes clear from the fact that AI adds to the morbidity and mortality of AIDS patient, and also early intervention in such patients prolongs as well as adds quality to life.

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