ORIGINAL ARTICLE

FREQUENCY OF ADRENAL INSUFFICIENCY AMONG PATIENTS OF HUMAN IMMUNODEFICIENCY VIRUS

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ABSTRACT

Background: Human immunodeficiency virus (HIV) has emerged as a major public health problem worldwide over the last two decades. Many complications and problems are associated with HIV like lipodystrophy, retarded growth in young patients, impaired endocrine and renal functioning and cardiovascular diseases.

Objective: To determine the frequency of adrenal insufficiency among patients of human immunodeficiency virus presenting to HIV clinic in a tertiary care hospital.

Methods: It is a cross sectional study conducted at HIV clinic, Jinnah Hospital Lahore during August, 2019 to February, 2020. A total of 180 patients of HIV presenting to HIV clinic of Jinnah hospital Lahore and fulfilling the selection criteria were approached after approval from ethical review board an informed consent was taken from the subject and an ACTH stimulation test was performed and adrenal Insufficiency was diagnosed. Intramuscular injection of 0.25 mg of synthetic ACTH was administered to all patients; and after 60 minutes serum cortisol was measured. A peak stimulated cortisol of less than 20 mcg/dl was labeled as adrenal insufficiency.

Results: Mean and standard deviation of the age was 42.16 ± 17.31 years. Male patients were 56.1% while female patients were 43.9%. Adrenal insufficiency was present in 38.3% patients while it was absent in 61.7% patients. No significant association found between age and presence of adrenal insufficiency (p=0.280). Also, no significant association found between duration of disease and adrenal insufficiency (p=.557). There was a significant association found between intake of antiretroviral therapy and presence of adrenal insufficiency having (p<0.005)

Conclusion: Adrenal insufficiency was found in significant number of HIV patients but effect modifiers like age, duration of disease did not show significant association except intake of antiretroviral therapy.

Key words: Adrenal Insufficiency (AI), Human Immunodeficiency Virus, Antiretroviral Therapy.

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INTRODUCTION

Human immunodeficiency virus (HIV) has emerged as a major public health problem worldwide over the last two decades.[1] The rate is showing a much steeper increase in developing countries due to socio economic factors like hunger, lack of education, poverty, presence of other diseases, lack of access to medical care and low socio-economic development.[2] According to the Pakistan National AIDS control program there are over one lac individuals suffering from HIV while the count is on a progressive rise. This has led to further burden on the health system of the country due to AIDS itself along with its treatment and long-term complications. Many complications and problems are associated with HIV like lipodystrophy, retarded growth in young

patients, impaired endocrine and renal functioning and cardiovascular diseases.[2] Adrenal insufficiency (AI) in HIV patients depends upon number of factors like extent of loss of adrenal function and rate at which it occurs, degree of stress and whether mineralocorticoid function is preserved. Due to insidious onset of adrenal insufficiency, it may go unnoticed until stress or an illness precipitates adrenal crisis.[3]

In patients with AIDS, primary adrenal insufficiency occurs in up to 20 percent. Fatigue is by far the most common presenting symptom. Only about one-third of the patients have hyperpigmentation and one-half have hyponatremia[4]. AI in patients with HIV/AIDS, is most common endocrine disease, and cause of high morbidity and mortality in these patients and they become severely ill due to adrenal crisis. AI among these patients is associated with different diseases and condition, like co-infection with Mycobacterium tuberculosis, cytomegalovirus, Kaposi's sarcoma, lymphoma and use of drugs such as rifampin. Relative cortisol deficiency is seen in HIV/AIDS patients with advanced disease mainly due to the decrease of cortisol reserves, that predisposes these patients to adrenal crisis at times of critical illness or stress.[3,5]

The prevalence of adrenal insufficiency is higher in developing as compared to developed countries during HAART era, perhaps due to lack of adequate facilities for an early diagnosis and inadequate treatments which predisposes them to the risk of opportunistic infections.[6] Various noninfectious conditions, infectious, and iatrogenic causes can obscure the clinical features and outcome of AI in these HIV/AIDS patients, which makes clinical diagnosis difficult. A screening algorithm to evaluate AI in these patients is required that may help clinicians to have an early diagnosis and treatment of AI in these patients. Majority of these HIV/AIDS patients with AI are either overlooked or diagnosed when disease process has been advanced in developing countries with limited resources. More research is needed to know the exact prevalence of AI in HIV/AIDS patients and extent of mortality in this population.

METHODS

A cross-sectional study was conducted from August, 2019 to February, 2020 at HIV clinic, Jinnah hospital Lahore. A total Sample size of 180 cases is calculated with 95% confidence level, 7 % margin of error and taking expected percentage of AI of 34.8% through a non-probability / consecutive sampling. Subject between 15 to 75 years of either gender of HIV positive with detection of human immunodeficiency virus (HIV) determined by PCR were included in the study. By doing an ACTH stimulation test, adrenal Insufficiency was diagnosed. Intramuscular injection of 0.25 mg of synthetic ACTH was administered to all patients; and after 60 minutes serum cortisol was measured. A peak stimulated cortisol of less than 20 mcg/dL was labeled as adrenal insufficiency. Patients on steroid therapy or taking rifampicin, and with known malignancy were excluded from the study. Data was entered and analyzed using SPSS version 23. Numerical variable i.e. age was summarized as mean and standard deviation. Qualitative variables like sex, presence of adrenal insufficiency was presented as frequency and percentage. Data was stratified for age, duration of disease and intake of antiretroviral therapy. Chi square test was applied to check statistical significance after stratification. P-value < 0.05 was taken as statistically significant.

RESULTS

The mean age was 42.16 ± 17.31 years. Mean duration of disease was 17.79 ± 7.01 months. Male patients were 101/180 (56.1%) while female patients were 79/180 (43.9%). Adrenal insufficiency was present in 69 (38.3%) patients. No significant association found between age group and adrenal insufficiency having ($p = 0.280$). There was no significant association between duration of disease and adrenal insufficiency ($p= 0.557$). There was a significant association between intake of antiretroviral therapy and presence of Adrenal insufficiency having ($p = <0.005$).

Table no: 1 Demographic and clinical profile of subjects

Variable n=180	Frequency	Percent
Age Mean =42.16±17.31 Years		
< 45	103	57.2
> 45 years	77	43.8
Gender		
Male	101	56.1
Female	79	43.9
Duration of disease Mean =17.79 ± 7.01 Years		
< 20 months	102	56.6
> 20 months	78	44.4
Presence of Adrenal insufficiency		
Yes	69	38.3
No	111	61.7

Table no: 2 Adrenal insufficiency and age, duration of disease and treatment cross tabulation:(n = 180)

Variables		Adrenal insufficiency		Total	P-value
		Yes	No		
Age	< 45 years	36	67	103	0.280
	≥ 45 years	33	44	77	
Duration of disease	< 20 months	41	61	102	.557
	≥ 20 months	28	50	78	
Intake of antiretroviral therapy	Yes	54	64	118	.005
	No	15	47	62	

DISCUSSION:

The present research conducted with an objective to determine the frequency of adrenal insufficiency among patients of human immunodeficiency virus presenting to HIV clinic of tertiary care hospital and one hundred and eighty cases were included by fulfilling the inclusion criteria by using non-probability consecutive sampling.

From 180 patients, it was observed that the minimum age was found 15 years and maximum age was 75 years with mean and standard deviation of the age was 42.16 ± 17.31 years. The minimum duration was 6 months and maximum were 30 months with mean and standard deviation of duration was 17.79 ± 7.01 months. Male patients were 56.1% while female patients were 43.9%. Adrenal insufficiency was present in 38.3% patients while it was absent in 61.7% patients. Adrenal insufficiency was present in 14.06% (9) HIV patients in another study, with a female to male ratio of 1: 3.5 and weight loss ($p<0.001$) and fatigue ($p<0.008$) were found to be statistically significantly associated with adrenal insufficiency[8]. In patients with HIV, adrenal insufficiency was high, and it was found to be associated with weight loss and fatigue[8].

There was no significant association between age group and presence of Adrenal insufficiency having p-value = 0.280. There was no significant association between duration and presence of Adrenal insufficiency having p-value = 0.557. There was a significant association between intake of antiretroviral therapy and presence of Adrenal insufficiency having p-value = <0.005. Existing studies described that the complex interaction between endocrine system and HIV infection may lead to decline in adrenal function slowly and ultimately leading to adrenal failure. Adverse endocrine outcomes are often precipitated by antiretroviral therapy as well as other essential medications. Besides adrenal insufficiency, AIDS wasting syndrome, diabetes mellitus, HIV lipodystrophy and hypo-gonadism need special reference. Endocrine evaluation should be done as in other patients with suspected endocrine dysfunction [8,9].

In a study by Bancos et al on diagnosis and management of adrenal insufficiency compared mean basal cortisol level among HIV and healthy controls and found a mean basal cortisol of 154.9 ± 27.2 nmol/L and 239.9 ± 31.6 nmol/L and the 30-minute post ACTH test cortisol mean values were 354.8 ± 19.9 nmol/L and 870.9 ± 163.5 nmol/L with increment mean cortisol levels were 200.0 ± 17.2 nmol/L and 631.0 ± 143.4 nmol/L among HIV as compared to healthy subject group respectively. All the values were statistically significant ($p<0.001$)[10]. The researcher used a diagnostic criterion in this study of 30-minute cortisol level <380.2nmol/L and increment from basal to stimulated cortisol level <158.5nmol/L and 34.8% patients with HIV were diagnosed with AI. Our study showed a frequency of AI in 38.3% of patients. Several studies have showing that clinically evident adrenocortical insufficiency is uncommon in persons with HIV[10,12,13] and evaluation of adrenal function among critically ill HIV/ AIDS patients is complex.

These recent studies suggest decreased cortisol breakdown among critically ill patients as the main contributing factor to elevated cortisol levels and there is need for a well-designed and large sample size research to explore early diagnosis, optimal evaluation and treatment of adrenal insufficiency in critically ill patients.[11]

In patients with HIV/AIDS, AI is one of the common endocrine manifestation and in developing countries, almost half of these newly diagnosed HIV and hospitalized HIV patient with advanced disease have AI and majority of these patients also have TB/HIV coinfection.[12] With almost 50% prevalence of adrenal insufficiency in patients with advanced HIV disease, it is worrisome that adrenal insufficiency diagnosis and evaluation is neglected in these patients that poses a

major contributing factors in morbidity and mortality in this population.[11-13]

CONCLUSION

Presence of Adrenal insufficiency was found in 38.3% patients with human immunodeficiency virus presenting to HIV clinic of tertiary care hospital. Effect modifiers like age, duration of disease did not show significant association except intake of antiretroviral therapy.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board of Allama Iqbal Medical College, Jinnah Hospital, Lahore via Reference No. IRB/21/2019 Dated: July 05, 2019.

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AUTHOR'S CONTRIBUTIONS

MS: Manuscript Writing
MA: Proofreading, review article
MAK: Data collection, Data analysis
RMA: Data analysis, Proofreading