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A COMPARATIVE STUDY TO FIND OUT THE PREVALENCE OF DIABETES MELITUS IN HAART PATIENTS WITH HIV- ASSOCIATED LIPODYSTROPHY AND WITHOUT HIV-ASSOCIATED LIPODYSTROPHY

Dermatology

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ABSTRACT

Background: HIV-associated Lipodystrophy (HAL) is a syndrome that occurs in HIV-infected patients who are being treated with antiretroviral drugs. Lipodystrophy is cosmetically disfiguring. Involvement of the face is most common and carries a social stigma, reducing the quality of life of patients with HIV disease. It also imposes a barrier to treatment and decrease adherence to ART medicines. These patients with are at increased risk for the development of diabetes mellitus and atherosclerosis. **Aim of the study:** To compare the prevalence of Diabetes Melitus in HAART (highly active anti retroviral therapy) patients with HIV-associated Lipodystrophy and without HIV-associated Lipodystrophy. **Materials and Methods:** After getting the patients consent, 52 HAART patients with Lipodystrophy were enrolled in group A and 62 HAART patients without Lipodystrophy were enrolled in group B. Blood samples for fasting and post-prandial blood glucose were taken from both the groups. **Results:** In group A, among the 52 patients enrolled, 15 were male (29%) and 37 female (71%). Predominant age group involved was 20-30 years. Patients on ZLN regimen were 37 (71%), TLE 12(23%) and ZLE 3(6%). Out of these, 7 (13.5%) patients had Diabetes Melitus. In group B, among the 62 patients enrolled, 31 were male (50%) and 31 female (50%). Predominant age group involved was 20-30 years. Patients on ZLN regimen were 44 (71%), TLE 13(21%), ZLE 4(6%) and TLN 1 (2%). Out of these, 11 (17.7%) patients had Diabetes Melitus. Chi-Square test was employed to find out the stastical difference of diabetic prevalence, but there was no such difference. **Conclusion:** This study has revealed that association of HIV associated Lipodystrophy does not influence the prevalence of Diabetes Melitus in HIV patients.

KEYWORDS:

HIV associated Lipodystrophy, Diabetes Melitus, HAART

Introduction

HIV-associated Lipodystrophy (HAL) is a syndrome that occurs in HIV-infected patients who are being treated with antiretroviral drugs. Global prevalence of HAL ranges from 10-80%.[1] Clinically it presents in three types; lipohypertrophy (fat accumulation), lipoatrophy (loss of fat tissue) and mixed type. Lipodystrophy is cosmetically disfiguring. Involvement of the face is most common and carries a social stigma, reducing the quality of life of patients with HIV disease. It also imposes a barrier to treatment and decrease adherence to ART medicines. [2, 3] Other features of HAL include hyperlipidemia, and hyperglycemia. Consequently, these patients with are at increased risk for the development of diabetes mellitus and atherosclerosis. Hence, we decided to find out the prevalence of Diabetes Melitus in HAL patients.

Materials and Methods

The study was conducted in a Link ART of a tertiary centre in Perundurai. Approval from the Ethical committee was obtained and after getting the patients consent, a total of 114 patients of age above 20 years, on HAART (highly active anti retroviral therapy) were enrolled. Among them, 52 HAART patients with Lipodystrophy were enrolled in group A and 62 HAART patients without Lipodystrophy were enrolled in group B. The details of the HAART Regimen were enclosed in Table 1.

	HAART REGIMEN			
	ZLN*	TLE*	ZLE*	TLN*
Group A (n=52)	37 (71%)	12(23%)	3(6%)	0
Group B (n=62)	44(71%)	13(21%)	4(6%)	1(2%)

*ZLN= Zidovudine, Lamivudine and Nevirapine
*TLE= Tenofovir, Lamivudine and Efavirenz
*ZLE= Zidovudine, Lamivudine and Nevirapine
*TLN= Tenofovir, Lamivudine and Nevirapine

Venous blood samples for fasting and post-prandial blood glucose were taken from both the groups and glucose level was analyzed by enzymatic method in auto-analyzer. HAL is a clinical diagnosis. Skin biopsy is not routinely performed to make a diagnosis of HAL.

Results

In Group A, among 52, 15 were male (29%) and 37 were female (71%). Age distribution of those 52 patients has been tabulated in Table 2.

Age Group	Number of patients
20-30	7(13%)
30-40	24(46%)
40-50	19(37%)
>50	2(4%)
Total	52(100%)

In Group B, among 62, 31 were male (50%) and 31 were female (50%). Age distribution of those 62 patients has been tabulated in Table 3.

Age Group	Number of patients
20-30	11(18%)
30-40	24(39%)
40-50	18(29%)
>50	9(15%)
Total	62(100%)

Table 4, show the duration of HAART in years for Group A patients.

Duration of HAART in Years	No. Patients	Percentage
10	7	13%
9	3	6%
8	1	2%
7	20	38%
6	18	35%
3	3	6%
Total	52	100%

Table 5, show CD4 Count Range in Group A

CD4 Count	No. Patients	Percentage
500-800	24	46%
200-500	11	21%
<200	17	33%
Total	52	100%

Table 6: HIV Associated Lipodystrophy with Diabetes Melitus Status Cross tabulation

			Diabetes Melitus Status		Total
			Yes	No	
HAL	Yes (Group A)	Count	7	45	52
		% within HAL	13.5%	86.5%	100%
		% within DM	38.9%	46.9%	45.6%
	No (Group B)	Count	11	51	62
		% within HAL	17.7%	82.3%	100%
		% within DM	61.1%	53.1%	54.4%
Total		Count	18	96	114
		% within HAL	15.8%	84.2%	100%
		% within DM	100%	100%	100%

Table 7: Chi -Square Tests

	Value	Df	Asymp Sig (2 sided)	Exact Sig (2 sided)	Exact Sig (1 sided)
Pearson Chi-Square	390 a	1	532	612	359
Continuity Correction b	134	1	714		
Likelihood ratio	393	1	531	612	359
Fischer's Exact Test				612	359
N of Valid Cases	114				

a = 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.21

b = computed only 2x2 table
The above tests revealed that there were no statistical difference for diabetic prevalence in group A and Group B.

Discussion

HIV-associated Lipodystrophy (HAL) is a syndrome usually seen in HIV-infected patients who are being treated with antiretroviral drugs. A cross-sectional study by Lichtenstein the prevalence of HAL in HAART (highly active anti retroviral therapy) was 49% [4]. Generally, protease inhibitors are associated with HAL, but Cheng et al [5] and brinkman et al [6] showed that treatment with NRTI also resulted in lipoatrophy.

The main mechanisms involved in HAL are; (i) ART regimens containing Protease inhibitors and Nucleoside reverse transcriptase inhibitors Stavudine and Zidovudine, (ii) genetic factors in the patients and (iii) HIV itself without ART. Patients with HAL are at increased risk for the development of diabetes mellitus and atherosclerosis. Hence, we decided to find the prevalence of diabetes mellitus in HAL patients.

The risk factors associated with HAL are [7] duration of ART therapy, older age, and low CD4 count.. Save et al study [8] male sex was only associated with HAL unlike our study where females were more common (71%). HAL was more common in older age group; 30-40 years=46% (n=24), 40-50 years= 37% (n=19) and >50 years= 4% (n=2). Majority of persons 46% (n=24) were in CD4 Count in 500-800, 21% (n=11) and in 33% (n=17) <200. Miller [9] et al study revealed that mean CD4 was 486 cells /milliliter. Tien PC [10] et al study longer cumulative exposure to NRTI was associated with increased DM incidence in HIV-infected women.

Reports from Brown et al [11] stated that incidence of Diabetes Melitus was four times more common in HAART than sero-negative patients. Initial report from Mehta study [12] has estimated a 5% to 7% cumulative incidence of DM in HIV-infected patients receiving HAART. In our study, we observed that diabetic prevalence in HAL was in 7 patients (n=20, 38%). Our study revealed that there was no statistical difference in Diabetic prevalence among the study group and control. To the contrary, Brar et al [13] finding has not showed an increased prevalence of DM in ART-naive HIV-infected patients. Studies by Muligen [14], Safrin [15] and Vigouroux et al [16] has suggested that metabolic changes precede morphologic changes in Lipodystrophy, so if we do periodical screening for altered blood glucose and lipid levels, we can avoid HAL at the earliest.

Lipodystrophy is often progressive and, in limited cases, may regress after the withdrawal of thymidine analogues (eg, switching from protease inhibitors to Efavirenz) has shown to be effective for reversing lipoatrophy. [17, 18] For lipohypertrophy, liposuction or lipectomy would be beneficial. For lipoatrophy, free flaps, lipotransfer, or commercial fillers or implants can be used to replace adipose tissue. Tesamorelin, a growth hormone–releasing factor analog, could be used to treat HAL. For the treatment of hyperlipidemia, drugs like fibrates and / or statins are used. [19] For treatment of hyperglycemia, metformin, insulin like growth factor–1,[20] are useful.

To conclude, early testing for metabolic alterations should be implemented at the initiation of HAART therapy even in the absence of clinical signs of Lipodystrophy. Still, more studies are needed to elucidate the most appropriate management for Lipodystrophy and glucose metabolism alterations and potential increase of cardiovascular risk.

References:

1. Alves MD, Brites C, Sprinz E. HIV-associated lipodystrophy: a review from a Brazilian perspective. TherClin Risk Manag. 2014. 10:559-66.
2. Huang JS, Lee D, Becerra K, Santos R, Barber E, Mathews WC. Body image in men with HIV. AIDS Patient Care STDS. 2006 Oct. 20(10):668-77.
3. Reynolds NR, Neidig JL, Wu AW, Gifford AL, Holmes WC. Balancing disfigurement and fear of disease progression: Patient perceptions of HIV body fat redistribution. AIDS Care. 2006 Oct. 18(7):663-73
4. Lichtenstein KA, Ward DJ, Moorman AC, et al; HIV Outpatient Study Investigators. Clinical assessment of HIV-associated lipodystrophy in an ambulatory population. AIDS 2001;15:1389-98.
5. Chen CH, Vazquez-Padua M, Cheng YC. Effect of anti-human immunodeficiency virus nucleoside analogs on mitochondrial DNA and its implication for delayed toxicity. Mol Pharmacol. 1991 May; 39(5):625-8.
6. Brinkman K, ter Hofstede HJ, Burger DM, Smeitink JA, Koopmans PP. Adverse effects of reverse transcriptase inhibitors: Mitochondrial toxicity as common pathway. AIDS 1998;12:1735-44
7. Schwenk A, Breuer JP, Kremer G, Römer K, Bethe U, Franzen C, et al. Risk factors for the HIV-associated lipodystrophy syndrome in a cross-sectional single-centre study. Eur J Med Res. 2000 Oct 30. 5(10):443-8.
8. Marianne Save`s. Factors Related to Lipodystrophy and Metabolic Alterations in Patients with HumanImmunodeficiency Virus Infection Receiving Highly Active Antiretroviral Therapy. Clinical Infectious Diseases 2002; 34:1396–405
9. Miller J, Carr A, Emery S, HIV lipodystrophy: prevalence, severity and correlates of risk in Australia. .HIV Med. 2003 Jul;4(3):293-301.
10. Tien PC, Schneider MF, Cole SR, et al. Antiretroviral therapy exposure and incidence of diabetes mellitus in the Women's Interagency HIV Study. AIDS. 2007 Aug 20;21(13):1739-45.
11. Brown TT, Cole SR, Li X et al. Antiretroviral Therapy and the Prevalence and Incidence of Diabetes Mellitus in the Multicenter AIDS Cohort Study. Arch Intern Med. 2005;165(10):1179-1184.
12. Mehta SHMoore RDThomas DLChaisson RESulkowski MS The effect of HAART and HCV infection on the development of hyperglycemia among HIV-infected persons. J Acquir Immune Defic Syndr 2003;33577- 584
13. Brar I, Shuter J, Thomas A, Daniels E, Absalon J; A comparison of factors associated with prevalent diabetes mellitus among HIV-Infected antiretroviral-naive individuals versus individuals in the National Health and Nutritional Examination Survey cohort. J Acquir Immune Defic Syndr. 2007 May 1;45(1):66-71.
14. Mulligan K, Grunfeld C, Tai VW, et al. Hyperlipidemia and insulin resistance are induced by protease inhibitors independent of changes in body composition in patients with HIV infection. J Acquir Immune Defic Syndr 2000; 23:35–43.
15. Safrin S, Grunfeld C. Fat distribution and metabolic changes in patients with HIV infection. AIDS 1999; 13:2493–505.
16. Vigouroux C, Gharakhanian S, Salhi Y, et al. Adverse metabolic disorders during highly active antiretroviral treatments (HAART) of HIV disease. Diabetes Metab 1999; 25:383–92.
17. Viganò A, Brambilla P, Cafarelli L, Giacomet V, Borgonovo S, Zamproni I, et al. Normalization of fat accrual in lipoatrophic, HIV-infected children switched from stavudine to tenofovir and from protease inhibitor to efavirenz. AntivirTher. 2007. 12(3):297-302.
18. Martínez E, García-Viejo MA, Blanco JL, Bianchi L, Buira E, Conget I, et al. Impact of switching from human immunodeficiency virus type 1 protease inhibitors to efavirenz in successfully treated adults with lipodystrophy. Clin Infect Dis. 2000 Nov. 31(5):1266-73.
19. Baldini F, Di Giambenedetto S, Cingolani A, Murri R, Ammassari A, De Luca A. Efficacy and tolerability of pravastatin for the treatment of HIV-1 protease inhibitor-associated hyperlipidaemia: a pilot study. AIDS. 2000 Jul 28. 14(11):1660-2.
20. Moses AC, Morrow LA, O'Brien M, Moller DE, Flier JS. Insulin-like growth factor I (rhIGF-I) as a therapeutic agent for hyperinsulinemic insulin-resistant diabetes mellitus. Diabetes Res ClinPract. 1995 Aug. 28 Suppl:S185-94.