Original Article

Study of clinical profile and outcome of venous thromboembolism associated with HIV infection in tertiary care center of Bharati Hospital, Sangli

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Abstract

Introduction: HIV infection predisposes to hypercoagulable state, it has been recognized as an independent risk factor for venous thromboembolism. **Material and Methods:** This is retrospective descriptive study of clinical profile and treatment outcome in HIV infection with venous thromboembolism. **Study period:** Feb. 2012 to 31 Jan 2015, during this period total 595 patients with HIV infection admitted in BVDUMC and H Sangli. Among this, was case series study of 8 patient had the diagnosis of venous thromboembolism, diagnosed by arteriovenous doppler study. The results of this study suggest HIV infection potentially develops venous thromboembolism (DVT), 2-10 times commoner in HIV infection than without HIV infection. Significant correlation between thrombotic disease and CD4+ count <200, as well as in the younger age group i.e. Age less than <45 years and mainly in females. **Conclusion:** Development of DVT in AIDS/HIV infection needs high index of suspicion to prevent, development of serious complication like PE, so as to prevent morbidity and mortality due to AIDS/HIV infection with VTE. Treatment is as per ACCP guidelines inj. Heparin (LMWH) sc bid for 5 days and oral anticoagulant Tab warfarin 5mg once a day or Dabigatran150mg twice a day continued for 6 months, monitoring with target INR between 2 to 2.5.

Keywords: Venous Thromboembolism, HIV/AIDS, DVT, Heparine.

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INTRODUCTION

Venous thromboembolism (thrombotic) disease has been recognized among human immunodeficiency virus / acquired immunodeficiency syndrome (AIDS) patients who have no clear cut general risk factors. The current incidence of VTE among HIV infected persons is estimated to be 2.6/1000-person/year[2]. And estimated rate of VTE is 0.1% in general population[1]. The overall risk of VTE in HIV infected patients was 2-10 folds higher than general population[2,3]. Most common involvement of venous thromboembolism (VTE) in HIV infected patients is popliteal and femoral vein and pulmonary artery and very rarely portal vein thrombosis. Recurrence rate of VTE is 8-15% in HIV/AIDS patients. Presentation of venous thromboembolism in HIV/AIDS patients mimics like opportunistic infection to rule out risk factors of VTE, such as advancing age, pregnancy, smoking, dyslipidemia, etc. Despite the fact that sub Saharan, Africa bears the greatest burden of HIV infection, but most reports of HIV DVT are from western world. Those are on HAART treatment on protease inhibitors, which interfere cytochrome p450, which up regulates thrombotic process, and generate endothelial and platelet dysfunction, also fat redistribution causes prothrombotic state.[5, 6,7] People living with HIV face an increased risk of deep vein thrombosis- potentially dangerous blood clots in major blood vessels, left undiagnosed and untreated DVT can cause pain, swelling and numbness, usually in the legs and can also travel to the pulmonary artery in the chest and causes life threatening blockage(pulmonary

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embolism). Various studies suggest that 1-2% of HIV positive people develop DVT at some point in their lives, which is a rate 10 times higher than expected among people without HIV[8]. This study is a case series of 8 cases of DVT during year of 1st February 2012 to 31st January 2015. Among all admitted and registered diagnosed cases of HIV at BVDUMC and H, SANGLI who had no apparent thrombotic risk factors. References suggestive of VTE and HIV infection occurs in mean age of 20-45 years in various studies.

MATERIAL AND METHODS

This is a retrospective study conducted at Bharati Vidyapeeth Deemed University Medical College and Hospital, Sangli, Maharashtra, a tertiary care centre. Prior to study institutional ethical committee permission was taken. A total no. of 593 RVD patients, age above 18years were admitted with HIV infection, out of which 8 were confirmed cases of VTE. Out of which 6 cases were DVT and one case of DVT with portal vein thrombosis and one case of DVT with increased D Dimer died due to PTE. Other common causes of VTE like advanced age, trauma, pregnancy, OCPs, surgeries and malignancies were excluded. Period of study was1st Feb 2012 to 31st Jan 2015. The cases of leg swelling with pain were investigated with arterio-venous Doppler study, having evidence of DVT were confirmed. However, in 4 patients DVT panel study was difficult because of expensive lab charges and unaffordability of the patients which was the limitation of the study. Epidemiological variables including gender, age, occupation and residential address were studied. The medical record of each patient was reviewed to identify whether the index VTE event represented as an incident (initial) or recurrent. Information was collected about patient's demographic characteristics, medical history, clinical characteristic, diagnostic test results and hospital management practices through review of medical records. Clinical manifestations were fever, cough, breathlessness, constipation and pain in abdomen, vomiting, pain and swelling of legs, chest pain. Laboratory data included all routine investigations, CD4 count, chest X ray, ECG, arterio-venous Doppler study, DVT profile wherever necessary. All confirmed cases of VTE were tested with ACCP guidelines 2012. Inj. Low Molecular Weight Heparin 0.6ml sc bd for 5 days with Vitamin K antagonist, oral anticoagulants- Tab warfarin 5mg OD to keep a target INR between 2-3. Therapy continued for 3 months of treatment course for first episode of VTE.

Table 1: Baseline characteristics of the patients

	Data	No. of cases	Percentage (%)
	Gender		
1	Male	03	37.5
	Female	05	62.5
	Age (in years)		
2	18-40	05	62.5
	41-60	03	37.5
	Occupation		
3	Farmers	02	25
	Housewife	05	62.5
	Businessmen	01	12.5
	Residence		
4	Rural	05	62.5
	Urban	03	37.5

Table 2: Symptoms and signs

	Symptoms/Signs	No. of cases	Percentage (%)
	Fever duration-		
1	1-3days	01	12.5
	4-7days	01	12.5
	>7days	03	37.5
2	Cough	01	12.5
3	Breathlessness	01	12.5
4	Constipation and pain in abdomen	01	12.5
5	Vomiting	01	12.5
	Pain in leg		
6	Right leg	05	62.5
	Left leg	02	25
7	Chest pain	01	12.5
8	Generalized weakness	05	62.5
9	Loss of appetite	01	12.5
	Risk factor		
10	OCP	-	
	Alcohol	01	12.5
	Smoker	-	
11	Altered mentation	01	12.5
12	Local temperature increased Left leg	04	50
13	Peripheral pulsation absent	01	12.5
14	ECG- Sinus Tachycardia	02	25
	CD4		
16	Less than 250	05	62.5
	250-400	03	37.5
	Venous Doppler study		
17	Extensive DVT from AVT /PVT uptoRt Iliac vein (Right leg).	01	12.5
	Portal vein Thrombosis with Rt leg.	01	12.5
	Left leg DVT	06	75
18	Lung crepitations	02	25

Table 3: Laboratory abnormalities

	Laboratory Data	No. of Cases	Percentage (%)
1	Anemia	03	37.5
2	Leucopenia	02	25
3	Leukocytosis	Nil	
4	Platelets <1.5lakh/mm^3	03	37.5
5	AST(SGOT)	Nil	
6	ALT(SGPT)	Nil	
7	ALP	Nil	
8	Sr. Creatinine	Nil	
9	D Dimer positive(>350ng/ml) Expired	01	12.5
10	USG Portal vein thrombosis	01	12.5
11	Chest X-Ray s/o Koch's	01	12.5
12	Serum homocysteine increased	01	12.5

RESULTS

A total of 8 patients were diagnosed cases of VTE from 01 Feb 2012 to 31 Jan 2015. All cases were confirmed with arterio-venous Doppler. The demographic results seen in table no.1 show that both males (n=3) and females (n=5) were among diagnosed VTE cases. Adults in this range of 18-40years constituted 05 cases (62.5%) and age 41 to 60 constituted 03 cases (37.5%). 05 patients (62.5%) were in the population. This study was done over a period of 2years. VTE with HIV is common in housewives may be because of fertility with hypercoagulable state and less mobility. 62.5% cases occurred in rural population. Clinical symptoms are shown in table no. 2 all patients have limb swelling, generalized weakness prior to hospital admission. Other symptoms were [1]fever (62.5%), generalized weakness(62.5%),loss of appetite (12.5%), cough (12.5%), breathlessness (12.5%),leg pain and swelling over leg (87.5%) pain in abdomen (12.5%),, chest pain (12.5%),absent peripheral arterial pulsations / oedema (87.5%),altered mentation (12.5%) and lung crepitations (12.5%). Laboratory values showed anemia (37.5%), leucopenia (25%), CD4 count <250/mm^3 (62.5%) and >250/mm^3 (37.5%), arterio venous Doppler study (87.5%), portal vein thrombosis (12.5%), tachycardia (25%), serum homocysteine levels raised (12.5%), one patient had acute breathlessness with D-Dimer value >350ng/ml and he expired due to PTE.

Etio-pathogenesis

Development of venous thromboembolism starts with acquired traditional risk factors such as advancing age, obesity (BMI>30), previous thrombosis, cigarette smoking, hypertension, immobilization, injecting IV drug, pregnancy and contraceptive pills and malignancies. Genetic risk factors associated with VTE are anti thrombin deficiency, protein c deficiency, protein s deficiency, factor v leiden and factor G20210A are responsible for development of VTE. Several multifactorial etiology are responsible for development of HIV related venous thromboembolism. These are viral risk factors such as CD4 <200 and detectable viral load. HIV infection itself causes a hypercoagulable state. It leads to protein s and protein c deficiency, anti thrombin deficiency, anti phospolipid syndrome, increased tissue factor (Sr. homocysteine, micro particles). HIV infection also causes vascular damage in the form of endothelial dysfunction leads to increased p selectin. There are increased chances of VTE associated with opportunistic infections such as cytomegalovirus, tuberculosis, pnuemocystisjiroveci infections. Also VT is associated with HIV related malignancies (Kaposi's sarcoma, non hodgkin's lymphoma and solid tumours). Iatrogenic factors responsible for development of VT in HIV infections such as indwelling catheters, surgery, drugs for ART treatment (protease inhibitors and megasterol acetate)

DISCUSSION

The array of the clinicopathologic spectrum related to HIV infection continues to increase and present new challenges to physicians caring HIV infected patients. Recent studies report of various abnormalities consistent with hypercoagulablestate leading to thromboembolic complications. The recent studies mentioned in African journal of primary health care suggest that reports of thrombotic disease among HIV infected patients who had no clear cut general risk factors. Various abnormalities leading to hypercoagulable state have been reported in patients with HIV who had thrombotic disease. Such abnormalities include the presence of anti phospholipids antibodies and lupus anticoagulants, protein c and protein s deficiency, increased levels of Von Wilebrand's factor and D Dimer. In our study these investigation were not possible because these facilities were not available in our centre. The abnormalities correlate with the HIV associated immunosuppression measured by CD4+ cells count and viral load associated with HIV infection. We emphasize that clinicians caring HIV patients need to be aware of thrombotic abnormalities and should consider PE in the differential diagnosis of hypoxia in these patients. Deep vein thrombosis was the commonest clinical presentation in the present case series;87.5%. both leg DVT. Other symptoms with decreasing order of frequency were pain and swelling over legs 62.5%, generalized weakness 62.5%, socio-demographic

characters such as in housewives (female) 62.5%, age between 18-40yrs (n=5) 62.5%, increased local temperature 50% cases, cough, breathlessness, vomiting, loss of appetite each 12.5% cases. The lab investigations in our study CD4+ count <250 (n=5) 62.5% associated with DVT and CD4+ count in the range of 250-400 (n=3) 37.5% cases. All clinically DVT patients undergone Arterio venous Doppler study, among Doppler study left leg DVT (n=6) 75% cases and right leg DVT, portal vein thrombosis each one i.e. 12.5% cases. Two patients having ECG showing sinus tachycardia 25% cases.(references 11,12,13 suggestive of DVT) We encountered one patients with portal vein thrombosis with DVT and other one patient with DVT with significantly raised D-dimer, who died due to PTE. All confirmed cases of VTE were treated with recommended DVT treatment, Inj low molecular weight heparin according to weight of the patient, 0.4-0.6 ml s/c bd for 5 days with oral anticoagulants continued for 3 months, monitoring INR 2-2.5 and all these patients are on ART regimen. Among 8 patients 7 patients responded to DVT treatment and they didn't have recurrence of DVT. There was one mortality because of late arrival in the hospital in serious complication.

CONCLUSION

HIV/AIDS infection and various abnormalities predisposing to a hypercoagulatle state leads to deep vein thrombosis/Venous thromboembolism (VTE) 2-10 times common in HIV infection. A high index suspicion may therefore be required to diagnose DVT/VTE and start early management to prevent serious complication like PTE leading to death, which decreases the mortality and morbidity.

REFERENCES

1. J ThrombHaemost 2007;5:692-9
2. Nigerian Medical Journal Vol. 52 Issue 2 April-June 2011
3. Mediterr J Hematol infect Dis. 2011;3
4. Thromb Res 1999 1;96:19-25 page
5. AIDS 2000;14:321-4
6. AIDS patient care STDs 2001:15:311-20
7. Rev Med interne. 2008;29:100-4
8. Journal of AIDS 1st July 2008 by John's Hopkins University School of Medicine
9. Sullivan PS, Dworkin MS, Jones JL, Hooper WC, and the Adult/Adolescent Spectrum of HIV Disease Project. Epidemiology of thrombosis in HIV-infected individuals. AIDS 2000; 14:321- 324.
10. Saber AA, Aboolian A, LaRaja RD, Baron H, Hanna K. HIV/AIDS and the risk of deep vein thrombosis: a study of 45 patients with lower extremity involvement. Am Surg. 2001 Jul; 67(7):645-7.
11. Jacobson MC, Dezube BJ, Aboulafia DM et al. Thrombotic complications in patients infected with HIV in the era of Highly Active Antiretroviral Therapy: a case series. CID 2004; 39: 1214-1222.
12. Copur AS, Smith PR, Gomez V, et al. HIV infection is a risk factor for venous thromboembolism. AIDS Patient Care STDS. 2002; 16:205-209.
13. Ahonkhai AA, Gebo KA, Streiff MB, et al. Venous thromboembolism in patients with HIV/AIDS. A case control study. J Acquir Immune DeficSyndr 2008; 48: 310-314
14. George SL, Swindells S, Knudson R, Stapleton JT. (1999). Unexplained thrombosis in HIV-infected patients receiving protease inhibitors: report of seven cases. Am. J. Med. 107, 624-626.
15. Fultz SL, McGinnis KA, Skanderson M, et al. Association of venous thromboembolism with human immunodeficiency virus and mortality in veterans. Am J Med. 2004; 116:420–423.

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