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Changing spectrum of renal disease in HIV

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ABSTRACT

The study was done to evaluate the spectrum of various renal histopathological lesions in patients infected with HIV (Human Immunodeficiency Virus).32 HIV positive patients underwent Renal biopsy over a period of 3 years from October 2013 to September 2016 who had presented with renal dysfunction and urine sediment abnormalities. Out of 32 patients, 24 were males and 8 were females. The mode of transmission of disease was sexual in 25 patients.14 patients presented with Nephrotic range proteinuria and 11 patients underwent RRT (renal replacement therapy). Majority of patients had tubulointerstitial lesions (18 patients) followed by glomerular lesions (14 patients).24 patients were receiving HAART (Highly active antiretroviral therapy) and majority of them had tubulointerstitial lesions. Hence Renal biopsy is indicated in HIV patients presenting with renal failure to arrive at proper diagnosis and treatment.

Key words: Human immunodeficiency virus, Highly active antiretroviral therapy, Renal replacement therapy, Renal biopsy.

INTRODUCTION

HAART in HIV patients has improved the survival as a result of which many of the diseases prevalent in normal population are increasing in this population. Even spectrum of renal manifestations has also changed in these patients. HIVAN (HIV Associated Nephropathy) which was common since two decades has been replaced by variety of tubulointerstitial and glomerular lesions. There is inadequate data from India with respect to histopathological lesions after introduction of HAART. Hence this study was carried out to study the spectrum of histopathological lesions in Renal biopsy specimens of HIV infected patients.

MATERIALS AND METHODS

Patients referred to Department of Nephrology from ART center at Outpatient Department along with patients admitted in Department of Medicine and Nephrology were enrolled for this study. Total of 68 patients were initially evaluated for renal dysfunction and 36 out of 68 patients eventually recovered and were not included in the study.32 patients with unexplained renal failure and proteinuria more than 1g/day underwent Renal biopsy.

Patients underwent detailed clinical evaluation, laboratory investigations and Renal Replacement therapy in the form of Intermittent Hemodialysis/ Sustained low efficiency dialysis when needed.

Renal biopsy was done under Real time Ultrasound guidance with 18guage, 18 cm (BARD) biopsy needle under local anesthesia .The samples were later subjected for Histopathology and Immunofluorescence.

RESULTS

During the study period a total of 32 cases were studied of which 24 were males and 8 were females. Mean age was 36±8.9 years. Fifteen patients were in category 1 (46.87 %), 10 in category 2 (31.25%) and 7 in category 3 (21.87%) based on the CDC Classification. Twenty four patients were on HAART therapy. Patients were initiated on HAART

regimen if they had AIDS defining illness, CD4 count less than 350 cells /microliter, acute HIV infection and symptomatic disease (HIVAN).HAART regimen included fixed dose combination of Zidovudine, Lamivudine and Nevirapine or Tenofovir, Lamivudine, Efavirenz.

Out of 32 patients, the probable mode of acquisition of HIV infection was sexual in 25 (78.12%) cases and non-sexual in 7 (21.87%) cases which include causes like exposure to contaminated blood products, perinatal transmission and IV drug abuse. The HIV status of partner was positive in 10 out of 32 (31.25%).The average duration of HIV infection by the time patients presented to our nephrology OPD was 11 years. Various systemic disorders associated with HIV renal disease are depicted in Table.2.

Laboratory investigations revealed mean serum creatinine of 4.2±3.2 mg/dl with average 24 hour urinary protein 2.4±1.9 gm/24 hours. Average CD4 count was 298/microliter.Sonological evaluation showed normal sized kidneys in 22 patients and bulky kidneys in 10 patients. Three patients were found to be Hepatitis B virus positive, 2 patients were positive for Hepatitis C virus, whereas one patient was positive for both Hepatitis B and Hepatitis C virus. Candidiasis was the most common opportunistic infection among the study group.

Eighteen patients presented with deranged RFT, out of which four patients underwent Renal Replacement Therapy (Hemodialysis + Sustained Low Efficiency Dialysis).Three patients were recovered , whereas one patient was dialysis dependant and was continued on maintenance hemodialysis. The histopathological lesions on renal biopsy specimen were depicted in Table no.3.Patients underwent renal biopsy with real-time ultrasound guidance under local anesthesia. Two biopsy samples were processed for light microscopy and immunofluorescence. The biopsy specimens were adequate with an average of twelve glomeruli. Tubulointerstitial lesions in the form of acute tubular necrosis, acute interstitial nephritis, chronic interstitial nephritis was the commonest finding. Two patients had crescentic glomerulonephritis and IgA nephropathy was seen in two patients. One patient had lupus like picture on light microscopy with a full house deposit on immunofluorescence (shown in Fig.no.1).Chronicity was noted in four patients in biopsy specimen.

Table: 1. CLINICAL PROFILE OF HIV PATIENTS

SEX Ratio	M:F = 24:8 (3:1)
Mean Age	36±8.9 Years
HIV Category 1 2 3	 15 10 07
HAART Therapy	24
Mode Of Transmission	Sexual = 25 Non Sexual = 7
HIV Status of Partner	10 POSITIVE
Duration of HIV Infection	11 Years

Table: 2. Systemic Disorders Associated with HIV Renal disease

RISK FACTOR	**No of patients**
Candidiasis	12
Tuberculosis	8
Hepatitis B	4
Hepatitis C	3
Type 2 Diabetes Mellitus	3
Herpes Zoster	2

Table: 3. Histopathology in HIV Renal Disease

HISTOPATHOLOGY	**No.of patients**
ATN	5 (15.60)
AIN	4 (12.50)
CIN	2 (6.25)
COLLAPSING FSGS	2 (6.25)
DN	2 (6.25)
Ig A Nephropathy	2 (6.25)
Crescentic GN	2 (6.25)
PIGN	2 (6.25)
MGN	2 (6.25)
MPGN	2 (6.25)
APN	1 (3.12)
CPN	1 (3.12)
TMA	1 (3.12)
MCD	1 (3.12)

Amyloidosis	1 (3.12)
FSGS	1 (3.12)
Lupus like lesion	1 (3.12)

HIV= Human immunodeficiency virus,AIN= Acute Interstitial Nephritis, ATN = Acute Tubular Necrosis, CIN = Chronic Interstitial Nephritis, PIGN = Post Infectious Glomerulonephritis, MGN = Membranous Glomerulonephritis, MPGN = Membranous GlomeruloNephrits, APN = Acute PyeloNephritis, CPN = Chronic Pyelonephritis, TMA = Thrombotic Microangiopathy, MCD = Minimal Change Disease, FSGS = Focal Segmental Glomerulo Sclerosis.

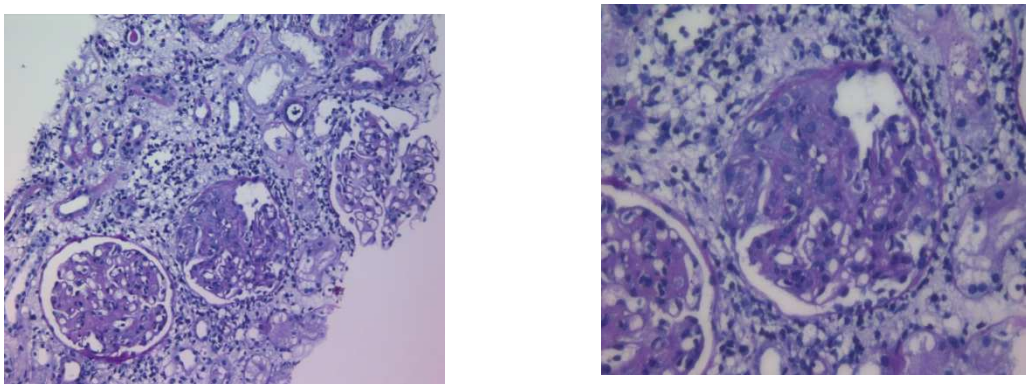

Fig No.1: Showing Lupus like lesion in patient with HIV infection.

DISCUSSION

Patients with HIV are at risk for both Acute Kidney Injury and Chronic Kidney Disease [1], secondary to medication nephrotoxicity and HIV associated Nephropathy(HIVAN) [2-5], Immune Complex kidney Disease [5-9] ,less commonly, kidney disease in the setting of Thrombotic Microangiopathy[10-11].In addition, the aging cohort of HIV positive patients may be at increased risk for kidney disease related to hepatitis B or C virus coinfection [5,2,13] and comorbid or treatment related diabetes or hypertension.

This 3 year prospective study done in our department shows a change in the prevalence of glomerular lesions with an increased proportion of Non HIVAN diseases compared to classical HIVAN seen in HIV Patients.

In our study, males outnumbered females in ratio of 3:1 whereas study by Peraldi.et al [14] male female ratio was 7:1 and Nigerian study the ratio was equivocal. In the study done by Vali.et al[21] in Osmania General Hospital, Hyderabad ,sex ratio was 6:1.

Transmission of HIV Infection is through different means including sexual exposure, exposure to contaminated blood products, perinatal transmission and IV drug abuse. In our study heterosexual contact is the main mode of transmission comparable to other studies [15].

Systemic disorders associated with HIV infection were seen in our study with Candidiasis being the most common followed by tuberculosis. This is comparable to study done by Peraldi et al[14].However Toxoplasma and Pneumocystis were less common due to Cotrimoxazole prophylaxis for patients with CD4 count less than 350/ microliter.

Renal disease in HIV patients has wide geographical variations, with prevalence being 2% among the HIV positive nephrotics in San Francisco, 15.2% in France[14]and 83% in a study by Bourgoignie et al[16]I.In our study fourteen patients presented with nephrotic range proteinuria, out of which only two patients had collapsing FSGS, which is in contrast to other studies [14,17,18,19] . Sonological evidence of bulky kidney was seen only in ten patients in our study which was common finding in patients with HIV associated kidney disease reported earlier. In our study tubulointerstitial lesions were the commonest histopathological lesions seen in approximately two-third of the patients, whereas glomerular lesions in remaining one-third. This is in sharp contrast to studies mentioned in the Table.4, where glomerular lesions were common and reflects the changing spectrum of histopathological lesions in patients with HIV on HAART therapy. Reason for this change in spectrum could be due to early referral to nephrologist in patients with renal dysfunction along with advancement in the renal biopsy technique with less complication rate, prolonged survival of the HIV infected patients.

In our study there was no correlation between the CD4 count and onset of renal dysfunction in HIV patients. This suggests that renal manifestations in HIV infection can present at any stage during the course of the illness.

Table.4 Histopathology in HIV renal disease- review of literature

STUDY	Number of patients	Glomerular lesions No (%)	*Tubulointerstitial* lesions No (%)	FSGS No (%)	MPGN NO (%)	MCD No (%)	Amyloid No (%)	DPGN No (%)	MN NO (%)
Columbia-Presbyterian Medical Centre [17]	104	93(89.4)	7(10.6)	73 (70.2)	10(0.6)	6(5.7)	3 (2.9)		
D'Agati.et.al[18]	136	127 (93.4)	9 (6.6)	88 (64.7)	13 (9.5)	6 (4.4)	4 (2.9)		
Madiwale et al.[19]				85%					
Peraldi et al. [14]				60%					
Janakiraman et al [15]	10	9 (90)		7(70)				1 (10)	1(10)
Verma[20]	25	14 (56)	3 (12)	4(33.3)	8(66.6)				
P.S.Vali et al [21]	27	15 (55.6)	11 (40.74) Vascular 3.7 %	Collapsing 3 (11.12) Other 2 (7.4)	1 (0.037)	1 (3.7)	3(11.12)	2 (7.4)	1 (3.7)
Our Study	32	14 (43.75)	18 (56.25)	1 (3.12)	2 (6.25)	1 (3.12)	1 (3.12)		1 (3.12)

HIV = Human Immunodeficiency Virus, FSGS = Focal Segmental Glomerulosclerosis, MPGN = Membranous Proliferative Glomerulonephritis, MCD = Minimal Change Disease, DPGN = Diffuse Proliferative Glomerulonephritis, MN = Membranous Nephropathy.

CONCLUSION

Renal disease in HIV patients is common. Previous studies have shown that glomerular disorders were predominant compared to tubulointerstitial disorders. In our study tubulointerstitial lesions were predominant which could be attributed to HAART therapy, prolonged survival, early referral to nephrologist and advancement in renal biopsy technique. Hence renal biopsy is indicated in all patients with HIV infection presenting with renal dysfunction for appropriate management.

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