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SPECTRUM OF NEPHROPATHY IN HIV PATIENTS: A SINGLE CENTER ANALYSIS

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ABSTRACT

Renal involvement is found to be common in HIV positive patients (17.3%), however Indian data are spare. The present study was done to find the spectrum of nephropathy in current scenario. Total number of cases are 19, in a two year study. Our preliminary results showed that collapsing glomerulopathy was not rare in Indian HIV positive population and also we have seen two cases of classical HIVAN in this study. Rest of the other cases are podocytopathies, immune complex-mediated glomerular disease, tubule-interstitial diseases.

Keywords: HIVAN- HIV associated nephropathy

INTRODUCTION

Worldwide, an estimated 37 million people are living with HIV infection. Kidney disease -major causes of morbidity and mortality in HIV-1 positive individuals. HIV-associated nephropathy (HIVAN), has become less common with widespread use of antiretroviral therapy (ART); however, there has been a simultaneous increase in the prevalence of other kidney diseases. Newer guidelines recommending earlier initiation of ART may further reduce the incidence of HIVAN, but the overall risk-benefit for kidney health is unknown. (1)

Naaz et al reported the first case of collapsing glomerulopathy in 2010 the state of Jammu and Kashmir which also happens to be a very low incidence belt for HIV. (2)

What is HIVAN in the age of current ART?

Typical presentation is heavy proteinuria and rapidly progressive renal failure.

Classic HIVAN is defined as collapsing glomerulopathy and attendant tubulointerstitial disease, including tubular microcyst formation, interstitial inflammation and tubular injury. (3).Glomerular "collapse": at least 1 glomerulus with collapse of glomerular basement membrane accompanied by hypertrophy and hyperplasia of the overlying glomerular visceral epithelial cells. These hyperplastic cells may fill the urinary space, forming pseudocrescent. (3)

Majority of these cases were found among blacks (Afro-Americans) heterosexual i.v. drug abusers. However, HIVAN was rare among white American homosexuals.(4-6) Studies from Europe have also found a low incidence of HIVAN in Caucasian and Asian patients as compared to blacks. (7-8)

The most common disorders include classic HIV associated nephropathy (HIVAN), HIV associated immune complex kidney disease (HIVICD) and HIV associated thrombotic microangiopathy (HIV-TMA). Nephrotoxicity associated with anti-retroviral therapy (ARV) and other therapies used to treat infections seen in HIV/AIDS are also an important consideration for renal failure in the setting of HIV infection. (9)

AIM

Analysis of the HIV associated nephropathies and its spectrum in a single tertiary care center of Maharashtra.

MATERIALS AND METHODS

- Data of renal biopsies of all HIV positive from 1s JAN 2017 to 1st JAN 2019 patients was analyzed. Patient >18 years of age having history of proteinuria and raised serum creatinine was studied. HIV positive diabetes and hypertensive patients are also included. Light microscopy and routine staining with H&E, PAS satin, sliver methenamine and Masson's trichrome. For immunofluorescence study phosphate buffer saline at pH -7.2 was used as a transport media. Sections of 4 µ thickness were stained with IgG, IgM, IgA, C3 & C1q antisera.

INCLUSION CRITERIA:

- All HIV positive patients of >18 years of age, having history of proteinuria and deranged renal function undergoing renal biopsies.
- Patients having associated diabetes and hypertension are also included in the study.

EXCLUSION CRITERIA:

All HIV positive patients < 18 years of age.

RESULTS

A total of 19 cases of renal biopsies were studied. Out of 19 patients 11 were males and 8 females. Most of the cases are of acute tubular injury with changes of benign hypertension (04/19, 21.0%), tubulo-interstitial nephritis (03/19,15.8%), chronic glomerulonephritis (03/19,15.8%), advanced diabetic nephropathies (03/19,15.8%), minimal change disease (02/19, 10.5%), membranoproliferative pattern (01/19,5.3%), crescentic glomerulonephritis (01/19,5.3%) and rare cases of classical HIVAN (02/19,10.5%) were also seen.

Diagnostic Features of HIVAN:

- **Light Microscopic Findings:-**
  - Collapsing glomerulopathy (segmental or global) with overlying visceral epithelial cell proliferation (pseudocrescent).
  - Microcystic tubular dilatation with active tubulointerstitial inflammation.
- **Immunofluorescence Findings:**
  - Absence of immune complex deposits.
- **Electron microscopic Findings:-**
  - Extensive foot process effacement
  - Tubuloreticular inclusions in endothelial cells

DISCUSSION

In this study, a total of 19 renal biopsies were performed. The majority of the patients were male (11 out of 19), while females accounted for 8 cases. Similarly, Vijay Gupta et al. (2013) conducted a pilot study in which 526 patients were screened, and 91 underwent renal biopsies. In that study, males were more frequently affected than females. The mean age of the patients was 36.5 years, with a range of 25 to 45 years. [10]

In our study, the most common histological finding was acute tubular injury, observed in 4 out of 19 cases. Tubulointerstitial nephritis was the next most common finding, present in 3 cases. Other notable diagnoses included diabetic nephropathy (2 cases) and HIV-associated nephropathy (HIVAN), also observed in 2 cases. These findings are significant and contribute important insights when compared with other studies. For instance, Varma P.P. et al. (2000) analysed 25 renal biopsies and reported mesangioproliferative glomerulonephritis in 08 patients, focal segmental glomerulosclerosis in 04, and collapsing glomerulonephritis in 01 patient. [11]

CONCLUSION

To conclude renal involvement was seem to be common in HIV patients. Screening of HIV associated renal lesions by renal biopsies is most important to known the histopathological spectrum of nephropathy. And as far as collapsing glomerulopathy (classical HIVAN) was concern, it was not a rare entity in Indian population.

TABLES

Table no.1 Findings of immunostaining in 19 patients with reference to light microscopy

Histology type	IgG	IgM	IgA	C3	C1q
HIVAN	Negative	Negative	Negative	Negative	Negative
Crescentic GN	Positive 3+, coarsely granular diffuse mesangial deposits, Focal in capillary wall	Negative	Negative	Positive 3+ , same as IgG	Negative
Acute GN	Positive 3+	Negative	Negative	Positive 3+	Negative
MPGN pattern	positive 3+, coarsely granular mesangial deposits	Negative	Negative	Positive 3+ , same as IgG	Negative
Minimal change disease	Negative	Negative	Negative	Negative	Negative

Table no. 2 Findings of immunostaining in 19 patients with reference to light microscopy

Histology type	IgG	IgM	IgA	C3	C1q
Chronic glomerulonephritis	Negative	Negative	Negative	Negative	Negative
Diabetic nephropathy	2+, interrupted linear deposits along CBM and TBM	Negative	Negative	Negative	Negative
Acute tubulointerstitial nephritis	Negative	Negative	Negative	Negative	Negative
Acute on chronic GN	Negative	Negative	Negative	Negative	Negative

Table no. 3, Comparative analyses of present study with other two studies.

S.no.	Comparative features	Vijay Gupta et al(2010) [8] N=26	J Prakash et al in 2015 [9] N=14	Present study(2018) N=19
1.	HIVAN	-	-	10.5%
2.	Collapsing FSGS	7.6%	Non collapsing FSGS - 14.2%	-
3.	Crescentic GN	-	7.14%	5.3%
4.	Acute GN	-		5.3%
5.	MPGN pattern	34.6%	35.7%	5.3%
6.	MCD	-	-	5.3%
7.	Chronic GN	11.5%	-	10.52%
8.	Diabetic nephropathy	-	7.14%	10.52%
9.	Acute tubulointerstitial Nephritis	15.3%	14.2%	15.8%
10.	Acute tubular injury	3.8%	-	31.5%
11.	TMA + ATN	7.6%	-	
12.	Diffuse mesangioproliferative	-	7.14%	-

IMAGES:

Fig.1 (a) Collapsing glomerulopathy, pseudocrescent, (b) HIVAN showing tubular microcystic dilatation, (c) Collapse glomeruli with pseudocrescent

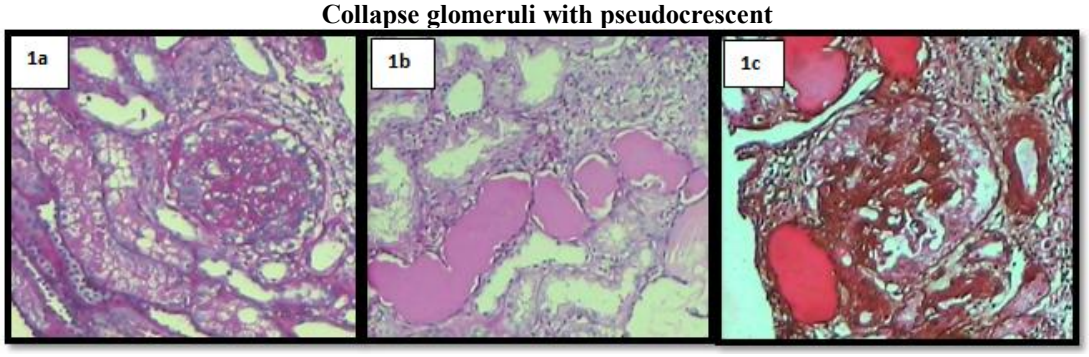


Fig.2(a) PAS stain of Crescentic glomerulonephritis, (b) Masson's trichrome, (c) IgG,(d) C3

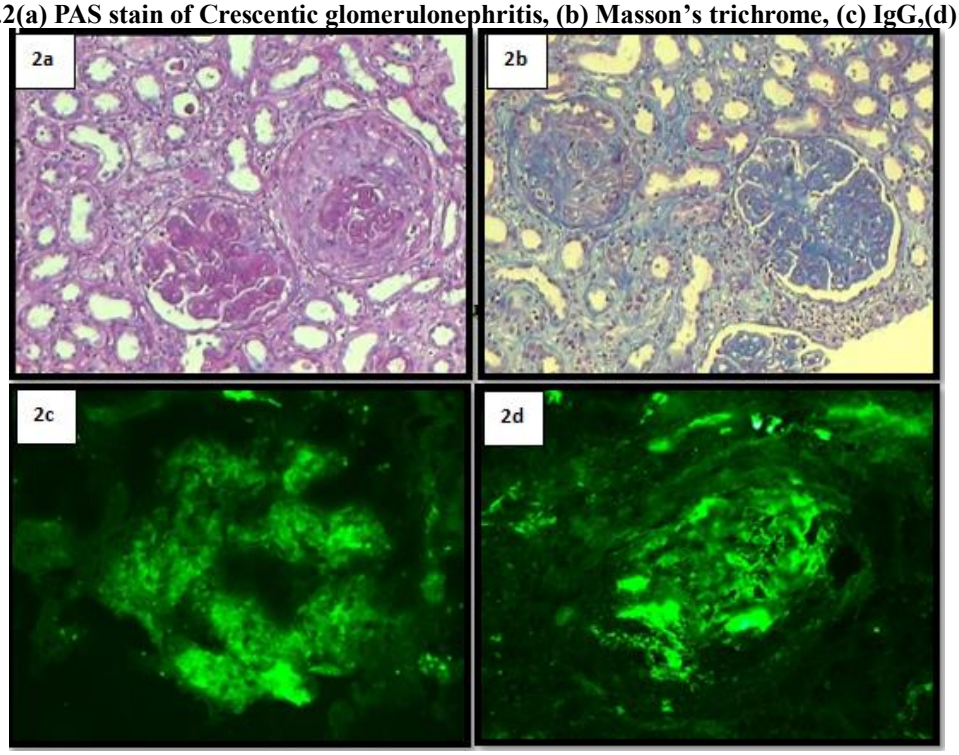
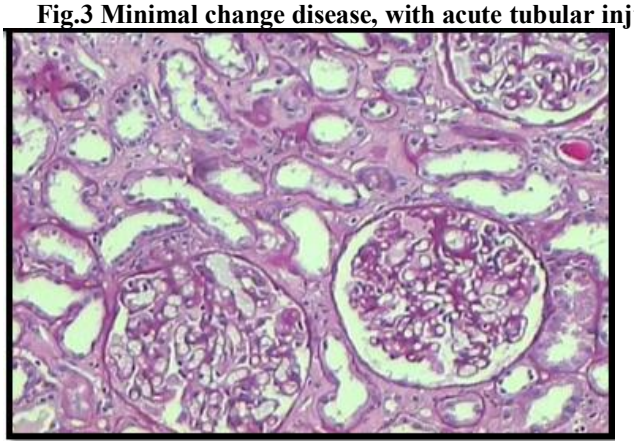


Fig.3 Minimal change disease, with acute tubular injury.



Glomeruli are enlarged in size and shows an occasional segmental area of increase in mesangial matrix & mild hypercellularity

Fig.4 Diabetic Nephropathy (a) MT stain, (b) Sliver stain

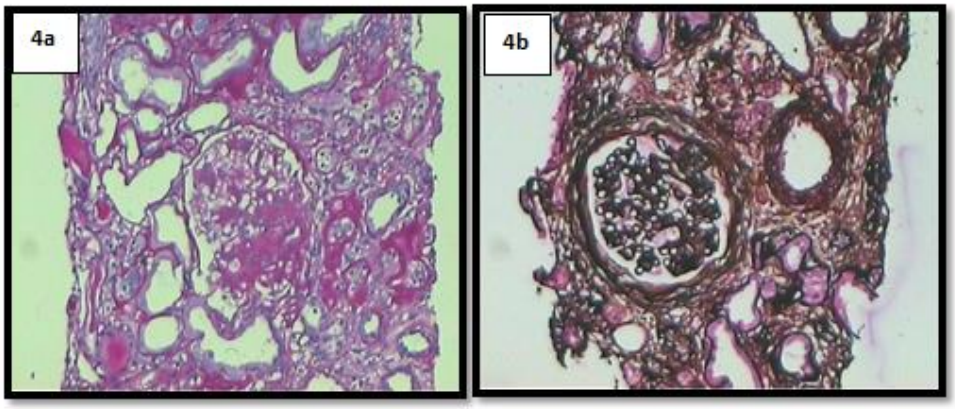


Fig.5 MPGN Pattern

Glomeruli show diffuse mesangial expansion. K-W nodules are seen in glomerulus. Diffuse thickening of capillary basement membrane with Periglomerular fibrosis is noted

Fig.6. MPGN pattern on immunofluorescence, (a) IgG. (b) C3.

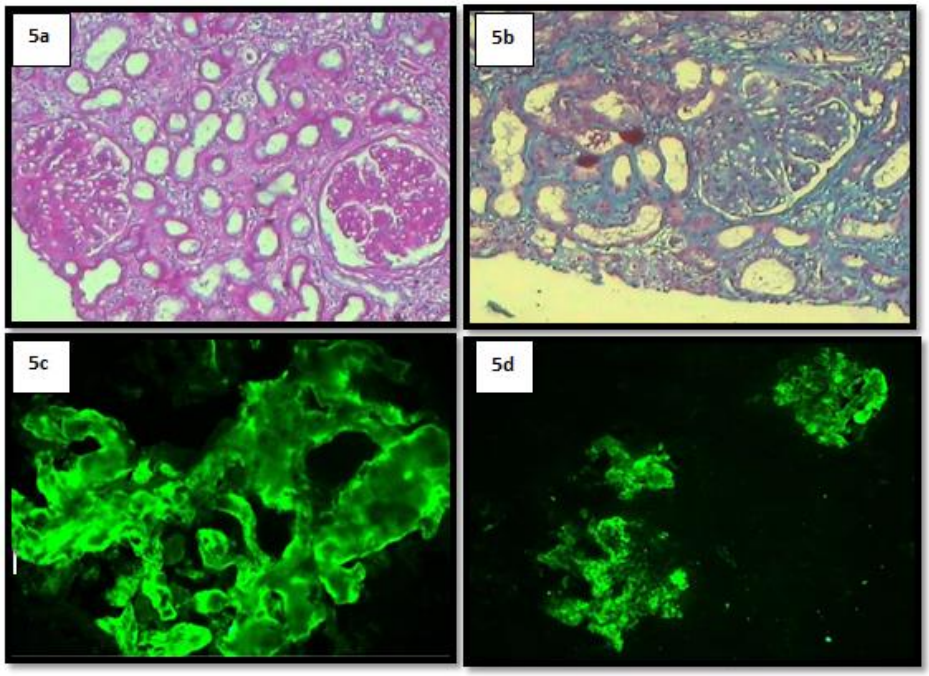


Fig.7 Acute tubule-interstitial nephritis

Glomeruli are enlarged in size & show diffuse mesangial & segmental endocapillary hypercellularity. Lobular accentuation glomerular basement membrane thickening & tram tracking is noted

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