

Morphological Patterns of Hepatitis C Virus (HCV) Associated Nephropathy in Lahore

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ABSTRACT

Background: Hepatitis C virus (HCV) is a hepacivirus. Hepatitis C virus (HCV) infection has been connected with numerous renal morphologies, including especially membranoproliferative and membranous glomerulonephritis. Affected patients present with microscopic/gross haematuria and or proteinuria.

Methods: Both children and adults were included in this study and a total of 132 consecutive patients of nephritic and nephrotic syndrome were studied. After initial investigations and considering the inclusion criteria, 30 (22.7%) cases were selected for this specific study. All cases were serum antigen positive for HCV.

Results: Amongst these 30 biopsies, 25 (83.33%) were males and only 5 (16.66%) were females. After analysis it was found that the least age at biopsy was 16 years and supreme was 55 years, mean \pm S.D of age was 36.53 ± 12.42 . Amongst the 30 patients, 12 (40%) presented with microscopical haematuria and macroscopical haematuria was found in 7 (23.3%) patients. Length for haematuria was 01-12 months with mean \pm S.D of 2.51 ± 2.8 . Proteinuria was observed in 29 patients, 13 (43.3%) had <2 g/day although 16 (53.3%) had >2 g/day proteinuria. Length for proteinuria was 1-16 months with mean \pm S.D of 4.78 ± 3.43 . Jaundice was not known in any patient. Out of 30 biopsies 6 (20%) were identified as membranoproliferative glomerulonephritis, 4 (13.3%) each were of diffuse proliferative nephritis, and end stage renal disease, 3 (10%) were focal mesangial proliferative nephritis. Diffuse mesangial proliferative nephritis and focal segmental glomerulosclerosis were also similar in percentage i.e. 3 (10%). Amyloidosis was confirmed by applying congo red stain and was 4 (13.3%), remaining 2 (6.7%) each were of diabetic nephropathy, and membranous glomerulopathy.

Conclusion: HCV can cause glomerulopathy and is related with a large spectrum of nephropathies. Membranoproliferative glomerulonephritis is a more common morphological pattern associated with HCV.

Key words: Glomerulonephritis, Hepatitis C virus membranoproliferative glomerulonephritis

INTRODUCTION

Hepatitis C virus (HCV) is RNA virus. it belongs to the family of Flaviviridae¹ it has become a main community anxiety because it has a high rate of chronic infection and results in cirrhosis and liver carcinoma. World Health Organization reported that approximately 170 million people about 3% of the world population, are infected with HCV. Hepatitis C virus (HCV) infection has been a cause of renal pathologies, including membranoproliferative glomerulonephritis and membranous GN³.

In 1993, just 4 years after the revelation of HCV, three autonomous gatherings in Japan, Italy and the US announced the identification of significant viral markers of contamination in patients with Type I membranoproliferative glomerulonephritis³. Even though the pathogenesis of HCV related glomerulonephritis isn't totally known so far the proposed pathogenesis depends on the reality of formation of cryoglobulins. These were considered in charge of the pathogenesis of kidney ailment and were recognized in about portion of the patients, subsequently uncovering that dominant part of patients with type II cryoglobulinaemia were, in fact, the casualties of HCV disease. Cryoglobulins prompt fundamental safe reaction to HCV⁴. Amyloid and immune complexes deposition as well chronic overstimulation of B-lymphocytes are other pathogenic mechanisms. Mixed cryoglobulins produced by HCV are primarily made out of a polyclonal immunoglobulin (Ig), either IgG or IgM, bound to another Ig act as anti-rheumatoid factor (RF).⁵ Glomerular harm then

can be because of decreased ability of monocytes to manage cryoglobulins⁶.

MATERIALS & METHODS

When renal biopsy was done, among 132 patients with different GN, thirty were observed to be serum anti HCV positive. A history, socio-statistic data was taken and physical examinations were performed. On each patient urinalysis was done. Tests for Serum HCV recognition, serum creatinine levels, ASO titre, ANF, anti DNA, serum supplement levels (C3 and C4) were done. Renal biopsies were taken by all around prepared nephrologists after assent from the patients and additionally guardians of the patient, in the event of a tyke. All patients had a place with Sheik Zayed Hospital, Services Hospital, Children Hospital, Jinnah, and Fatima Memorial Hospital Hospital Lahore.

RESULTS

Amongst these 132 patients 30 renal biopsies were HCV antibody positive, among them, 25 (83.33%) were males and 5 (16.66%) were females. The minimum and maximum age is shown in the table

Among the 30 patients of hepatitis C positive patients, 4 (3%) gave a background marked by taking blood transfusion while 1 (0.8%) had a contracted liver. Jaundice was not reported in any patient. Lowest serum creatinine was 0.60 mg/dl and extreme was 15.50 mg/dl with a mean \pm S.D was 3.87 ± 3.90 mg/dl. Serum bilirubin ranged

from 1.80 g/dl to 6.10 g/dl and showed mean \pm S.D of 4.45 \pm 0.89g/dl. Each biopsy was stained with Haematoxylin-eosin stain. For Mesangial network, mesangial cells, vessels and basement membrane, Periodic acid Schiff's (PAS) was applied. Additionally Congo red to picture amyloid stores, Masson's trichrome to see the degree of fibrosis and Jones Methenamine silver stain for the discovery of changes of GBM was applied. The results were as follows:

Among 30 renal biopsies, 6(20%) were diagnosed as membranoproliferative GN, 3(10%) each were focal mesangial proliferative nephritis, diffuse mesangial proliferative nephritis, focal segmental glomerulosclerosis and amyloidosis, 4(13.3%) each were of diffuse proliferative nephritis, and end stage renal disease, 2(6.7%) each were of diabetic nephropathy, and membranous nephropathy.

Table 1:Age of 30 patients in relation to sex

Sex of patient	Mean	Number	Std. Deviation	Minimum	Maximum	Range
Male	37.92	25	11.885	16	55	39
Female	29.60	5	14.153	17	53	36
Total	36.53	30	12.428	16	55	39

Table 2:Duration of Haematuria (in months)in 30 patients

Gender	Mean	N	Std. Deviation	Minimum	Maximum	Range
Male	3.78 \pm 0.68 (95% CI=2.32-5.25)	25	2.85511	1	12.00	11.00
Female	5.00 \pm 1.00 (95% CI=7.7-17.70)	5	2.82843	4	6.00	2.00
Total	2.5167	30	2.81156	1	12.00	11.00

Among 30 patients, 29 showed proteinuria, 13 (43.3%) had $<$ 2g/day while 16 (53.3%) had $>$ 2g/day. Duration of proteinuria was minimum 1 month and maximum was 16 months with mean \pm S.D of 4.78 \pm 3.43.

Table 3:Duration of Proteinuria (in months) in 30 patients

Sex of patient	Mean	N	Std. Deviation	Minimum	Maximum	Range
Male	4.6 \pm .58 (95% CI=3.4-5.8)	25	2.75785	1.00	12.00	11.00
Female	6.5 \pm 3.28 (95% CI=3.9416.93)	5	6.55744	1	16.00	15.00
Total	4.7833	30	3.43833	1	16.00	15.00

DISCUSSION

Hepatitis C virus infection has been linked with membranoproliferative and membranous GN. Though the precise mechanism of disease is not completely well-known as yet the proposed pathogenesis by most researchers is based on the fact that there is production of circulating cryoglobulins. These were believed to be responsible for the disease and were detected in about half of the patients, thereby enlightening relationship between type II mixed essential cryoglobulinaemia and HCV infection. Cryoglobulins cause systemic immune response to HCV.⁴ Cryoglobulins prompt fundamental safe reaction to HCV. 4 Amyloid and immune complexes deposition as well chronic overstimulation of B-lymphocytes are other pathogenic mechanisms.⁵ Glomerular destruction then can be because of decreased ability of monocytes to cope cryoglobulins⁶.

The range of renal pathology related with HCV disease thus extended to incorporate numerous examples in native and transplanted kidneys.⁷ An ongoing report on renal biopsies, got just before liver transplantation showed twenty five from 30 patients had HCV related immune complex GN. MPGN being 40%⁸.

The cryoglobulins and HCV antigen-counter acting agent edifices are normally accused in the pathogenesis of HCV nephropathy; anyway they can't clarify all the detailed sores. This brings up the issue whether the infection can prompt renal damage by direct cytopathic impact. In fact, the kidney is flawlessly fit the bill to be an objective for HCV contamination. It has the

apparatus required for grip and endocytosis, receptors that are fit for conveying the infection intracellularly, and the cell arrangement required for replication.⁹ Results of our study are in harmony with different other studies.^{8, 10, 11} HCV related renal ailment is uncommon in kids. It normally shows up in patients with long standing disease. It is regularly connected with gentle subclinical liver disease¹².

In 14 available series on the pervasiveness of HCV in primary MPGN, the occurrence of HCV was 15%, which is meaningfully advanced than in general population. Conversely the occurrence was greater (96%) when patients had both positive cryoglobulinaemia and HCV positivity¹⁵. MPGN is unequivocally connected with endless HCV disease and ought to be suspected all around firmly when a HCV positive patient indicates proteinurea, hypocomplementemia and cryoglobulinaemia

In another investigation roughly 80% patients with HCV related MPGN had no manifestations of liver disease.¹⁶ Patients with MPGN type I for the most part present with proteinuria, regularly with the nephrotic disorder, microscopical haematuria, and shifting degrees of renal deficiency. Hypocomplementaemia, principally included early parts of the established pathway, is likewise common.¹³

In another study, at Sheikh Zayed hospital Lahore, to check efficacy of antiviral therapy in HCV associated glomerulopathy, studied 30 patients who were reported from 30th June 2004 to Feb. 2007. Renal biopsy results showed mesangial proliferative glomerulonephritis (7%)¹¹. Data concerning association of HCV with DPGN is scant and in the form of case reports. Horikoshi et al 1993

announced that a 62-year-elderly person with hepatitis C infection (HCV) disease showed proliferative glomerulonephritis.¹⁶ likewise Uchiyama-Tanaka, in 2004 revealed an instance of HCV related membranous nephropathy¹⁷.

Epidemiological analyses have recommended a linkage between sort 2 diabetes and incessant hepatitis C infection (HCV) contamination. In the HCV transgenic mice, the capacity of insulin to bring down the plasma glucose level was impeded. This is like the discoveries, as saw in ceaseless hepatitis C patients. These results make available a direct experimental evidence for the input of HCV in the development of insulin resistance in human HCV infection. HCV infection, in end principals to the rise of type 2 diabetes¹⁸.

In this study, 3 (10%) renal biopsies showed amyloidosis, all (100%) were males. Cryoglobulinaemia caused by HCV stimulate monoclonal B-cell proliferation through chromosomal reorganization. This could be resulted resulted from HCV infection. This chromosomal reordering, may have led to production of amyloid proteins, nonetheless additional study is needed to check this suggestion¹⁹.

The long term result of HCV-related nephropathies stays hazy. Succeeding cross-sectional examinations demonstrated that HCV-positive patients had a 40% higher plausibility for creating renal inadequacy characterized as higher serum creatinine of 1.5 mg/dl contrasted with the seronegative subjects. There is expanded danger of renal malady movement just as, the general forecast for patients with HCV-related nephritis is poor as a result of a high frequency of co-contaminations and cardiovascular ailment²⁰.

To our knowledge the present study, is the first study, covering clinical, biochemical, morphological details of HCV associated glomerulonephritis from Pakistan. Many venues are yet to be explored in HCV associated glomerulonephritis. Large scale multicentre studies are needed to explore further including, epidemiological, clinical, biochemical, morphological, immunofluorescence, immunohistochemical as well as genetic aspects required to find further details of HCV associated GN in our country. In addition electron microscopical studies can be more revealing hence efforts may be directed to explore HCV ribonucleic acid in kidney tissue of HCV infected patients.

Conflict of notice is none.

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