Hepatitis B virus serum markers and Clinico-pathological characteristics of Hepatitis B virus associated Glomerulonephritis (HBV-GN)

Yin Yin Mon, Khin Khin Win, Khin Thida Thwin

Department of Nephrology, University of Medicine-1, Yangon.

Background:

HBV-associated glomerulonephritis is common in area of high prevalence of HBV infection and immune-complex glomerulopathy was generally accepted as pathogenetic mechanism.

Objective:

To find out the association between hepatitis B viral serum markers and clinico-pathological characteristics of the patients with HBV-associated glomerulonephritis

Methods:

This is a hospital based cross sectional descriptive study involving 36 HBV-associated GN patients from Yangon Specialty Hospital and ThingangyunSanpya General Hospital within one year and six months period.

The HBV serum markers were measured by using immunoassay.

Methods:

Their clinical characteristics, pathological types and HBcAg deposit in renal biopsies (by immunohistochemistry method), then find out their association with serum HBeAg.

Results:

All patients were chronic hepatitis B infection and

serum HBeAg positivity was 30.6% and

anti-HBe positivity was 30%.

Pathological types of HBV-GN among study population

Types of GN	Frequency	Percentage
Minimal change	11	30.6
Membranous GN	6	16.7
Mesangioproliferative GN	12	33.3
Membranoproliferative GN	7	19.4
Total	36	100.0

Clinical characteristics	Number	Percentage (%)
Renal function		
Stage I	16	44.4
Stage II	9	25.0
Stage III	9	25.0
Stage IV	2	5.6
Stage V	0	0
Proteinuria		
< 3.5 g/dl	5	13.9
≥ 3.5 g/dl	31	86.1

Clinical characteristics	Number	Percentage (%)
Microscopic hematuria		
<2 rbc/hpf	15	41.7
≥2 rbc/hpf	21	58.3
Hypertension		
Present	9	25
Absent	27	75
Serum transaminase level		
Raised	7	19.4
Normal	29	80.6

Association between clinical characteristics and serum HBeAg

	serum HBeAg			
Renal function stages	Positive	Negative	Total	p value
Stage I	6 (54.5%)	10 (40.0%)	16 (44.4%)	0.031
Stage II	0 (0.0%)	9 (36.0%)	9 (25.0%)	
Stage III	3 (27.3%)	6 (24.0%)	9 (25.0%)	
Stage IV	2 (18.2%)	0 (0.0%)	2 (5.6%)	
Stage V	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Proteinuria				0.123
< 3.5 g/dl	3 (27.3%)	2 (8.0%)	5 (13.9%)	
≥ 3.5 g/dl	8 (72.7%)	23 (92.0%)	31 (86.1%)	

	serum HBeAg			
Microscopic Hematuria	Positive	Negative	Total	p value
< 2 rbc/hpf	6 (54.5%)	9 (36.0%)	15 (41.7%)	0.298
≥ 2 rbc/hpf	5 (45.5%)	16 (64.0%)	21 (58.3%)	
Blood pressure				
<140/90 mmHg	5 (45.5%)	22 (88.0%)	27 (75.0%)	0.007
>140/90 mmHg	6 (54.5%)	3 (12.0%)	9 (25.0%)	
Transaminase levels				
normal	6 (54.5%)	23(92.0%)	29 (80.6%)	0.009
raised	5 (45.5%)	2 (8.0%)	7 (19.4%)	

There was statistically significant association between serum HBeAg & renal function (p =0.031), hypertension (p =0.007) and serum transaminase levels (p =0.009).

There was no significant association between serum HBeAg & nephrotic range proteinuria (p =0.123) and microscopic hematuria (p =0.298).

Association between types of HBV-GN and glomerular deposition of HBcAg

	HBcAg in renal tissue	
Type of GN	Positive	Negative
Minimal change	0	11
Membranous GN	0	6
Mesangioproliferative GN	0	12
Mebranoproliferative GN	0	7
Total	0	36

Discussion:

In this study, the demographic characteristics of the patients were comparable to other studies.

Clinical characteristic of HBV-associated glomerulonephritis patients

According to the studies by Jiang & Liu (2008) and Zhang et al., (2010), there was association between renal injury and HBV DNA replication.

In this study, serum HBV-DNA level had not done. The replication of virus had been predicted by serum HBeAg instead of HBV-DNA

And serum HBeAg positive group had more renal function impairment, hypertension and raised serum transaminase levels than negative group.

Pathological types of HBV-glomerulonephritis

According to the international data analysis of Hepatitis B virus-associated nephropathy by Khedmat & Taheri (2010),

- membranous GN was more common in children and
- IgA nephropathy was common in adult.

In the study by Raveendran et al (2017), different types of GN were

- Membranous GN (37.6%),
- Membranoproliferative GN (18.75%),
- FSGS (18.75%) and
- IgA nephropathy (12.5%) respectively.

In the clinical study by Panomsak et al (2006),

- IgA nephropathy (29%),
- Membranous GN (21%),
- FSGS (11%),
- Membranoproliferative GN (11%) and
- post-infectious GN (11%) respectively.

Chen et al (2008) stated that

- Membranous GN (66.7%)
- Mesangioproliferative GN (33.3%)

In the study by Zhang et al., (2012), the types were

- Mesangioproliferative GN (24.9%),
- Membranoproliferative GN (19.5%),
- IgA nephropathy (15.5%),
- Membranous GN (11.6%),
- Minimal change disease (9.4%)
- other types (10%) respectively.

In this study, the most common type is mesangioproliferative glomerulonephritis

Association between serum HBeAg and types of HBV-GN

Although it has been reported that there was association between types of GN and HBV, the exact pathogenetic mechanism was unknown.

Four major mechanisms had been suggested,

- cytopathic collision,
- deposition of immune complex containing viral antigen,
- virus induced specific immunological mechanism and
- indirect effect of virus induced cytokines.

Depending on the size and charge of immune-complex, the deposition of immune-complex were differed.

The smaller size of HBeAg and cationic nature of anti-HBe which tend to attract the sub-epithelial localization of immune deposit in membranous glomerulonephritis.

In contrast, larger size of HBsAg and anionic nature of anti-HBs favor mesangial localization in IgA nephropathy.

In membranoproliferative GN, there is both sub-epithelial and mesangial deposition of HBeAg.

In the present study, serum HBeAg positivity was

- 30.6% for all types of HBV-GN and
- 45.5% for mesangioproliferative GN and
- 27.3% for both membranoproliferative GN and minimal change disease.

On analyzing the data from this study, we can’t predict the type of GN by serum HBeAg status.

It may be due to some factors like variation in immune responsiveness to the diverse HBV antigens, size and charge properties of HBV antigen, geographical pattern of HBV prevalence among different regions of the world.

We can explore these factors by doing larger sample size in the future.

Association between serum HBeAg and clinical characteristics of the patients

In this study, GN patients with serum HBeAg positive group were more likely to have renal impairment, hypertension and raised transaminase levels but degree of proteinuria, microscopic hematuria, were not significantly differed from those of HBeAg negative patients.

Association between HBV antigen in renal tissue (HBcAg) and type of glomerulonephritis

HBeAg is part of viral nucleoprotein derived from denatured HBcAg.

In pediatric HBV-related MN, HBeAg was detected in 95% of glomerular deposit but no HBcAg and HBsAg in these deposits.

Serum HBeAg was also positive in 93% of the patients.

Lai et al (1991), reported that 76.1 % (16/21) of adults with HBV-related membranous nephropathy had depositions of HBeAg along glomerular capillary wall and 23.9% of patients had HBcAg depositions respectively.

In this present study, there was no glomerular deposition of HBcAg in all patients.

It may be due to fluctuating HBcAg level, low serum concentration of HBV-DNA or HBcAg, the sensitivity of detection methods or small sample size.

The frequency of detection of HBV antigen would be greater if we use all HBV antigens (HBsAg, HBeAg, HBcAg) including HBV-DNA.

It will be more informative if we use RT-PCR following RISH method.

Underlying immunological abnormality, viral genetic mutation and genetic predisposition should be considered in HBV-GN pathogenesis. So we need further study to explore this factors

Conclusion:

There was some association between HBV serum markers and clinical characteristics (renal function, blood pressure and transaminase levels) of HBV-associated glomerulonephritis.

So in area of high prevalence of HBV infection, the viral markers are important in their management.

THANK YOU