

# *Acta Medica Okayama*

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*Volume 38, Issue 1*

1984

*Article 12*

FEBRUARY 1984

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Albumin receptors on HBsAG particles and  
subsequent sero-conversion designate  
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active liver disease patients.

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# Albumin receptors on HBsAg particles and subsequent sero-conversion designate HBeAg-positive patients among chronic active liver disease patients.\*

Takao Tsuji

## Abstract

An enzyme-linked immunosorbent assay (ELISA) for the purpose of detecting the albumin receptor on hepatitis B virus surface antigen (HBsAg) particles was developed. Patient sera with moderate to high receptor values demonstrated significant correlations with serum DNA-polymerase activity ( $p$  less than 0.005), but not with HBeAg titer. Within one year of the study of 47 HBeAg-positive patients, only in the group of 12 patients with the moderately high values and 9 with low values, did 2 (16.7%) and 6 cases (66.7%) sero-convert, respectively. These results suggest that the albumin receptor might be a useful marker of HBsAg-positive patients.

**KEYWORDS:** albumin receptor, HBV, HBeAg, sero-conversion of HBeAg, chronic active hepatitis

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\*PMID: 6322527 [PubMed - indexed for MEDLINE]

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— BRIEF NOTE —

**ALBUMIN RECEPTORS ON HBsAG PARTICLES AND  
SUBSEQUENT SERO-CONVERSION DESIGNATE  
HBeAg-POSITIVE PATIENTS AMONG  
CHRONIC ACTIVE LIVER  
DISEASE PATIENTS**

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*Received November 16, 1983*

*Abstract.* An enzyme-linked immunosorbent assay (ELISA) for the purpose of detecting the albumin receptor on hepatitis B virus surface antigen (HBsAg) particles was developed. Patient sera with moderate to high receptor values demonstrated significant correlations with serum DNA-polymerase activity ( $p < 0.005$ ), but not with HBeAg titer. Within one year of the study of 47 HBeAg-positive patients, only in the group of 12 patients with the moderately high values and 9 with low values, did 2 (16.7 %) and 6 cases (66.7 %) sero-convert, respectively. These results suggest that the albumin receptor might be a useful marker of HBsAg-positive patients.

*Key words :* albumin receptor, HBV, HBeAg, sero-conversion of HBeAg, chronic active hepatitis.

Since the initial discovery by Matsushashi and Hosokawa in 1972 (1), many investigators have confirmed that sera from liver disease patients react with glutaraldehyde-treated polymerized human serum albumin (pHSA) (2-4). This reactivity is observed more frequently in HBsAg-positive sera, being associated predominantly with HBeAg (2, 3). It also correlates with the prognosis of acute hepatitis type B (4), and increased vertical transmission of hepatitis B virus (HBV) (3). In the present study, a sensitive enzyme-linked immunosorbent assay (ELISA) for the detection of the albumin receptor on HBsAg particles (5) was developed.

Serum samples were obtained from 20 healthy persons, 65 asymptomatic HBV carriers and 79 HBsAg-positive and 30 HBsAg-negative patients with chronic active liver disease (CALD). Of these latter 109, 8 were histologically diagnosed as chronic persistent hepatitis (CPH) type B, 35 as chronic active hepatitis (CAH) type B, 30 patients as CAH type non-A·non-B, and 36 patients as liver cirrhosis type B. Patients with HBsAg-positive sera were divided into 3 groups : a) HBeAg-positive, b) anti-HBe-positive, and c) neithers. HBeAg-positive patients were followed for 12 to 24 months. HBsAg, anti-HBs, HBeAg, and anti-HBe were

detected by standard RIA methods (Abbot Laboratories, U.S.A.). Serum DNA-polymerase activity was measured by the method of Kaplan *et al.* (6). PHSA was prepared according to Lenkei and Ghetie (7). Horseradish peroxidase (HRP)-labelling of pHSA and ELISA, for quantitation of pHSA-binding activity (pHSA-BA), was accomplished by a previously reported method (5). Anti-HBs-coated microplates were prepared according to the method of Wolters *et al.* (8), and a quantitative assay for the detection of pHSA-BA (5) was developed. Recognized pHSA-BA was represented by an optical density (OD) ratio, and calculated as follows :

$$\text{Value (OD ratio)} = \frac{\text{OD of test sample} - \text{OD of blank II}}{\text{OD of blank I} - \text{OD of blank II}}$$

Blank I was the average OD of 10 healthy controls, and blank II that of background.

The mean pHSA-BA values of HBeAg-positive group (group a) was  $104.3 \pm 18.5$  in asymptomatic carrier,  $105.0 \pm 7.1$  in CPH patients,  $97.8 \pm 17.5$  in CAH, and  $86.5 \pm 18.5$  in liver cirrhosis (no significant differences). In anti-HBe-positive (group b) or HBeAg- and anti-HBe-negative (group c) groups, the pHSA-BA mean

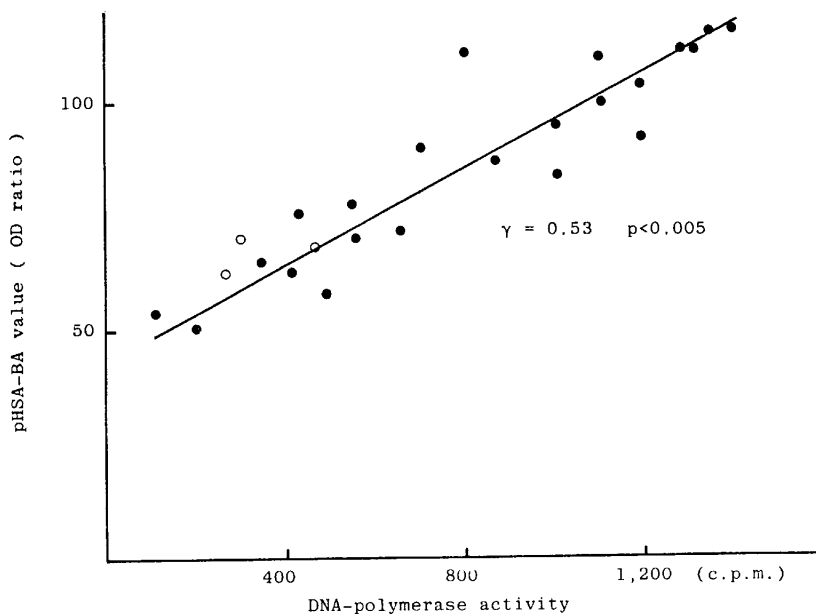


Fig. 1. The activities of DNA-polymerase in 22 HBeAg-positive (●) and 3 both HBeAg- and anti-HBe-negative (○) patients with high or moderately high pHSA-BA value (more over 50 OD ratio).

TABLE 1. ALBUMIN RECEPTOR ACTIVITIES AND SERO-CHANGES OF HBeAg IN HBeAg-POSITIVE PATIENTS WITH CALD<sup>a</sup>.

pHSA-BA values(OD ratio)	No. of CALD patients	No. of patients with sero-changes of HBeAg after 1 year	
		No. to anti-HBe-positive	No. to both HBeAg- and anti-HBe- negative
More over 90	26	0	0
90-50	12	2 (16.7)	2 (16.7) <sup>b</sup>
Under 50	9	6 (66.7)	1 (11.1)

<sup>a</sup> CALD : chronic active liver diseases. <sup>b</sup> Numbers in parentheses indicate percentage.

values in each disease were significantly lower than in the HBeAg-positive groups. The serum samples with moderate to high pHSA-BA values (ratio over 50) from 22 HBeAg-positive and 3 HBeAg- and anti-HBe-negative CAH patients, were correlated significantly DNA-polymerase activity ( $p < 0.005$ ) (Fig. 1). Sero-changes with one year in 47 HBeAg-positive patients with CALD (27 with CAH and 20 with liver cirrhosis) are shown in Table 1. Twenty-six patients with high pHSA-BA ratios (over 90) did not sero-convert, but 4 of 12 patients with moderately high values (50-90) did, 2 cases to anti-HBe-positively and 2 to HBeAg- and anti-HBe-negative. In patients with low pHSA-BA values (under 50), 7 of 9 converted, 6 cases to anti-HBe-positively, and 1 to HBeAg- and anti-HBe-negative. All 8 patients who converted to anti-HBe-positive patients presented good clinical progress, but the 3 patients with HBeAg- and anti-HBe-negative result did not improve with clinical findings of slight liver injury persisting.

These results suggest that the HBV receptor for polymerized human serum albumin (pHSA) might be a useful marker of HBeAg- positivity in patients with chronic active liver diseases.

*Acknowledgements.* The author wishes to express his profound thanks to Prof. Dr. Takahiro Yamabuki and Miss Suzue Mimura of Health Research Center, Okayama University for his encouragement and her technical assistance.

This work was supported by Grant-in-Aid (No. 58570321) for Scientific Research from the Ministry of Education, Science and Culture of Japan in 1983.

#### REFERENCES

1. Matsushashi, T. and Hosokawa, A.: Reactants to human serum albumin-coated red blood cells found in Au (1)-positive sera. *Jpn. J. Exp. Med.* **42**, 183-184, 1972.
2. Imai, M., Yanase, Y., Nojiri, T., Miyakawa, Y. and Mayumi, M.: A receptor for polymerized human and chimpanzee albumins on hepatitis B virus particles co-occurring with HBsAg. *Gastroenterology* **76**, 242-247, 1979.
3. Stevens, C.E., Neurath, A.R., Szmuness, W., Beasley, R.P. and Ikram, H.: Correlations between HBeAg/anti-HBe, HBsAg titer, HBsAg-associated albumin binding sites and infectivity. ed. GN. Vyas, SN. Cohen, and R. Schmid, In *Viral Hepatitis*. The Franklin Institute Press, Philadelphia, pp. 211-216, 1978.
4. Pontisso, P., Alberti, A., Bortolotti, F. and Realdi, G.: Virus-associated receptors for polymerized

- human serum albumin in acute and chronic hepatitis B virus infection. *Gastroenterology* **84**, 220-226, 1983.
5. Tsuji, T.: Detection of serum albumin receptor in hepatitis B virus carriers by enzyme-linked immunosorbent assay. *Gastroenterol. Jpn.* **17**, 585-590, 1982.
  6. Kaplan, P.M., Gerin, J.L., Purcell, H. and Greenman, R.L.: DNA polymerase associated with human hepatitis B antigen. *J. Virol.* **12**, 995-1005, 1973.
  7. Lenkei, R. and Ghetie, V.J.: Methods for detection for anti-albumin autoantibodies in hepatic diseases. *J. Immunol. Methods* **16**, 23-30, 1977.
  8. Wolter, G., Kuijper, L., Kačaki, J. and Schuurs, A.: Solid-phase enzyme-immunoassay for detection of hepatitis B surface antigen. *J. Clin. Pathol.* **29**, 873-879, 1976.