# SERUM HAPTOGLOBIN CONCENTRATIONS IN ACUTE HEPATITIS A

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# INTRODUCTION

The serum haptoglobin (Hp) which is a part of the  $\alpha_2$ -globulin in the serum protein is a glycoprotein. Hp is known to be biosynthesized in hepatic cells, but it is still difficult to explain exactly about the mechanism of Hp pathway within hepatic cells. Some observations had been reported about specific changes of the serum Hp concentrations in cases of inflammatory diseases and hepatic diseases.

In the early summer of 1984 many people in some parts of Miyazaki prefecture suffered from hepatitis A. Fourteen patients were admitted and treated in the National Sanatorium Miyazaki Hospital. The serum Hp concentrations of these patients of acute hepatitis A were measured during different stages of the disease. The investigations are reported herein.

# MATERIALS AND METHODS

From April to August on 1984 reported cases of acute hepatitis A had increased in a part of Miyazaki province. Fourteen patients, 9 males and 5 females with acute hepatitis with jaundice were admitted and treated in the Miyazaki Hospital.

The "A" type of acute hepatitis was diagnosed by an examination of immunoglobulin (total-HA antibody and HA-Ig M antibody) and serum biochemical data. Total-HA antibody was interpreted by an inhibition method and HA-Ig M antibody was represented by cut off index. Serum Hp was measured by a single radial immunodifusion method (Nyman, 1959). Standard values of serum biochemical data and also standard values of concentration of serum Hp were measured from 15 normal individuals.

#### RESULTS

HA antibody of hepatitis A patients are shown in Table 1. Mean values of HA-Ig M antibody in the early clinical stage of acute hepatitis A were  $7.28 \pm 1.71$  (Mean-SD).

#### Table 1

HA antibody in patients with hepatitis A.

Patient No	HA-Ig M antibody (cut off index)					
	early clinical	healing				
100.	stage	stage				
1.	7.7	3.7				
2.	10.4	5.5				
3.	7.3	3.9				
4.	7.2	6.4				
5.	9.0	5.8				
6.	5.7	6.5				
7.	8.2	4.1				
8.	6.4	4.3				
9.	5.8	5.6				
10.	6.5	3.4				
11.	6.0	6.9				
12.	8.5	5.1				
13.	6.4	6.4				
14.	6.8	5.2				
M±SD	7.28 ± 1.71	5.23 ± 1.31				

Total HA antibody positive.

cut off index > 1.0: positive cut off index < 1.0: negative

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## Table 2

Serum biochemical data of 15 normal subjects and 14 hepatitis A patients. (M  $\pm$  SD).

	T-bil	D-bil	GOT	GPT	LDH	Cho-E
St. values	$0.52 \pm 0.18$	0.23 ± 0.11	20.3 ± 9.3	17.7 ± 8.1	254.1 ± 83.1	$0.86 \pm 0.15$
Early clinica	al stage					
Pat.	T-bil	D-bil	GOT	GPT	LDH	Cho-E
No.	0-1.0 mg/di	0-0.4 mg/dl	8-40 U	5-35 U	50-440 U	0.6-1.2∆ph
1.	18.0	16.5	584	628	762	0.36
2.	12.3	10.9	560	661	627	0.41
3.	7.5	6.3	285	302	524	0.60
4.	10.8	9.4	468	526	846	0.43
5.	7.2	6.1	248	285	483	0.59
6.	14.2	12.8	424	588	680	0.38
7.	18.1	16.2	751	820	562	0.43
8.	11.9	10.9	486	511	748	0.54
9.	8.0	7.2	292	368	468	0.52
10.	10.1	8.8	300	394	448	0.65
11.	14.1	12.6	384	421	524	0.23
12.	16.5	15.1	618	726	642	0.53
13.	10.5	8.9	406	541	688	0.61
14.	6.3	5.5	281	303	548	0.48
In healing st	age					
1.	1.2	0.4	33	40	382	0.98
2.	0.6	0.1	21	27	186	1.02
3.	0.5	0.3	32	25	220	1.18
4.	0.8	0.2	18	19	420	1.14
5.	0.6	0.1	30	38	162	1.15
6.	0.9	0.3	24	26	263	0.89
7.	1.2	0.1	17	29	164	1.21
8.	0.6	0.1	22	18	264	1.50
9.	0.6	0.3	20	18	125	1.03
10.	0.8	0.1	25	35	264	0.97
11.	0.7	0.3	18	30	122	1.15
12.	0.8	0.1	16	28	168	1.20
13.	0.7	0.2	26	32	214	1.05
14.	0.7	0.2	24	27	138	1.20

In the healing stage of the disease these values decreased to  $5.23 \pm 1.31$ .

Serum biochemical data of standard values of 15 normal subjects and all cases, in the early clinical stage and in the healing stage of acute hepatitis A are shown in Table 2.

Standard values of serum Hp were  $132.47 \pm 27.39 \text{ mg/dl}$  (Table 3). In the early clinical stage of acute hepatitis A mean serum Hp values, which were  $100.57 \pm 25.20 \text{ mg/dl}$ , were significantly lower than standard. Mean serum Hp values in the healing stage of the disease were  $128.36 \pm 29.83 \text{ mg/dl}$  and these

## Table 3

Serum haptoglobulin in patients with hepatitis A. (Standard : 132.47 ± 27.39 mg/dl)

Dationt	Serum haptoglob	oulin (mg/dl)		
No	early clinical	healing		
1.0.	stage	stage		
1.	94.6	122.4		
2.	102.8	124.9		
3.	105.3	126.7		
4.	101.7	131.7		
5.	110.0	136.2		
6.	96.4	131.4		
7.	96.8	120.4		
8.	102.7	135.0		
9.	106.1	119.7		
10.	103.2	132.5		
11.	89.7	131.3		
12.	98.0	135.2		
13.	101.1	123.2		
14.	99.6	126.4		
$\overline{M \pm SD}$	$100.57 \pm 25.20$	128.36 ± 29.83		

Standard vs early clinical stage : p < 0.01 Standard vs healing stage : N.S. early clinical stage vs healing stage: p < 0.01 N.S. : Not significant

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values were significantly higher than those in the early clinical stage. There was no difference between those values in the healing stage of the disease and standard.

#### DISCUSSION

It has been observed and reported that serum Hp decreased or disappeared in chronic liver diseases (Williams and Wemyss, 1961). In a case of a fulminant hepatitis, against an increase of transaminases, serum Hp decreased. It was reported that serum Hp also decreased in a case of liver transplantation. According to these data serum Hp would be biosynthesized in hepatic cells (Hanley et al., 1983; Chew et al., 1984). It was experimentally observed that the <sup>14</sup>C-leucine was found within a part of haptoglobin after intravenous perfusion of <sup>14</sup>C-leucine in the liver (Baumann and Jahreis, 1983; Straten et al., 1984). The whole amount of these <sup>14</sup>C-leucine were demonstrated in hepatocytes. A protein synthesizing ability in the liver could be known by measuring the concentration of the haptoglobin (Haugen et al., 1981; Hooper et al., 1981). It was observed that concentration values of serum Hp were higher in cases with acute inflammation than normal subjects. In the another report serum Hp values increased in cases of an aortic syndrome (Okada et al., 1980).

The liver would be affected by severe inflammation in the early clinical stage of acute hepatitis A, and in the healing stage serum values were significantly lower than standard. Those data showed Hp biosynthesis in the liver were increasing with the improvement of the disease. In the healing stage of acute hepatitis A values of serum Hp increased and no significant difference was found between those values of patients and standard. These values of serum Hp could be an indicator of the stage of acute hepatitis A.

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It was difficult to know why many cases suffered from acute hepatitis A in this area. But it was a very interesting fact that all patients had eaten fresh oysters without cooking some weeks before clinical signs of acute hepatitis. It is a popular custom in this area to catch oysters on the coast and to eat them raw. It was uncertain but one could discuss about contaminated oysters as a possibility of a source of infection of acute hepatitis A.

### SUMMARY

The serum haptoglobin (Hp) values of patients of acute hepatitis, whose serum total-HA antibody in the early clinical stage of the disease were positive, had been investigated. In thee arly clinical stage of these patients of acute hepatitis A mean serum Hp values were  $100.57 \pm 25.20 \text{ mg/dl}$ . These values were significantly lower than standard. Hp values of patients gradually increased to the standard values during improvement of the disease. Mean values of Hp in the healing stage of these patients were  $128.36 \pm 29.83$  mg/dl, and there was no significant difference between values in this stage of the disease and standard. But a significant difference was seen between serum Hp values in those two stages of acute hepatitis A.

In this study it was observed that the ability of the Hp biosynthesis in hepatic cells had decreased in the early clinical stage of acute hepatitis A, and it recovered in the healing stage. Serum Hp values could be an indicator in the stage of acute hepatitis A.

### ACKNOWLEDGEMENTS

The author wishes to extend appreciation to many staffs of the National Sanatorium Miyazaki Hospital.

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