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Incidence and Clinical Significance of Mitochondrial Glutamic Oxaloacetic Transaminase in Blood Serum in Patients with Liver Diseases

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In 1960, two glutamic oxaloacetic transaminases were separated by paper electrophoresis. One of these was of mitochondrial origin (GOT_m) and the other was confined to the cytoplasm (GOT_s). It is more difficult to liberate GOT_m into blood serum than GOT_s and it is suggested that GOT_m activity can be elevated in blood serum only when the liver is severely injured. Therefore, the incidence and the clinical significance of GOT_m in blood serum must be investigated.

In 13 patients (68%) in the florid stage of acute viral hepatitis, the activity of serum GOT_m was in the 30—40 IU range, while the activity of GOT_m was slight during convalescenece. In 8 patients (32%) with chronic aggressive hepatitis, the activity of serum GOT_m was in the10—20 IU range and in 2 patients (16%) with chronic persistent hepatitis, 22 patients (81%) with fatty liver, and 9 patients (19%) with liver cirrhosis, serum GOT_m activity was generally less than 10 IU.

Based on these findings, it can be said that serum GOT_m activity can be recognized in patients with acute and chronic diseases of the liver. The mechanism of the appearance of GOT_m in blood serum and the clinical significance of GOT_m remain unsolved.

(Key words: GOT_s, GOT_m, hepatitis, fatty liver)

INTRODUCTION

The estimation of the deviations of glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) in blood serum, which are related to natural cellular fermentation, principally reflects fermentation deviations due to injured parenchymal cells of the liver and the extent of elevated transaminase activity in blood serum suggests the liver cell injury in general. At present, therefore, a test for elevation of the activity of serum transaminase is the most widely used method for evaluation of liver damage.

In 1960, two glutamic oxaloacetic transaminases were separated by paper electrophoresis. One of these was of mitochondrial origin (GOT_m) and the other was confined to the cytoplasm (GOT_s) (1). It is more difficult to liberate GOT_m into blood serum than GOT_s and it is suggested that GOT_m activity can be elevated in blood serum only when the liver is severely injured. Therefore, the appearance and clincial significance of GOT_m in blood serum must be investigated.

This paper describes the appearance of GOT_m in the blood serum in liver diseases in practice.

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MATERIALS AND METHODS

GOT_m activity in the blood serum was examined in 19 patients with acute viral hepatitis, 25 patients with chronic aggressive hepatitis, 12 patients with chronic persistent hepatitis, 27 with fatty livers, 46 with liver cirrhosis, 12 with nonspecific reactive hepatitis, 3 with intrahepatic cholestasis, 4 with hepatoma, 4 with metastatic cancer of the liver and 16 healthy persons as controls.

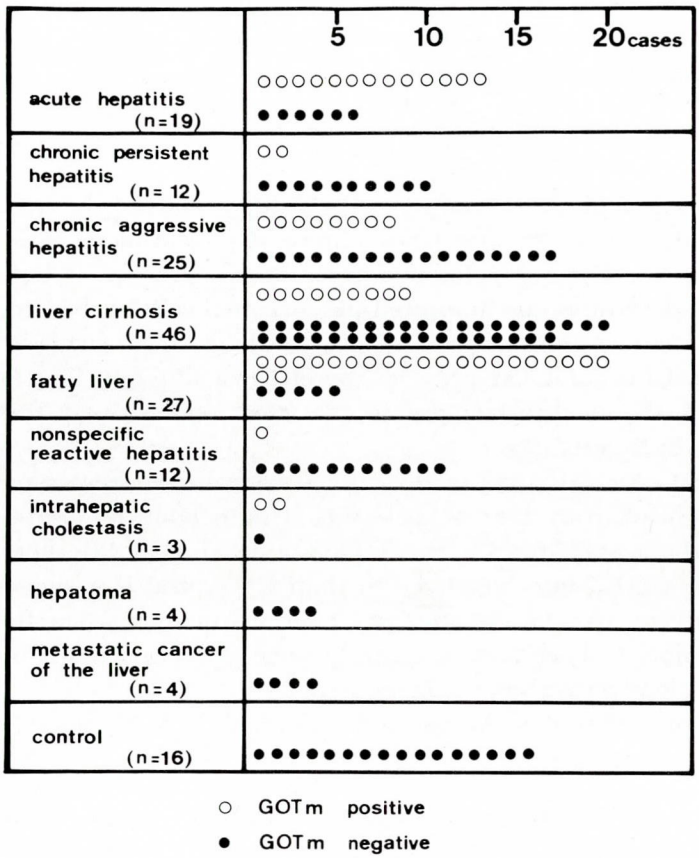
For the separative assay of GOT isozyme, the method of plate electrophoresis and diazonium salts according to Katsunuma et al. was used (2).

RESULTS

(I) Incidence of GOT_m activity in blood serum (Table 1)

In 13 (68%) of 19 patients with acute viral hepatitis, 8 (32%) of 25 with chronic aggressive hepatitis, 2 (16%) of 12 with chronic persistent hepatitis, 22 (81%) of 27 with fatty liver, 9 (19%) of 46 with liver cirrhosis, one (8%) of 12 with nonspecific reactive hepatitis, and 2 (66%) of 3 with intrahepatic cholestasis, investigations of serum GOT_m activity showed positive results, while GOT_m activity in blood serum was negative in patients with primary and metastatic cancer of the liver as well as in the control group.

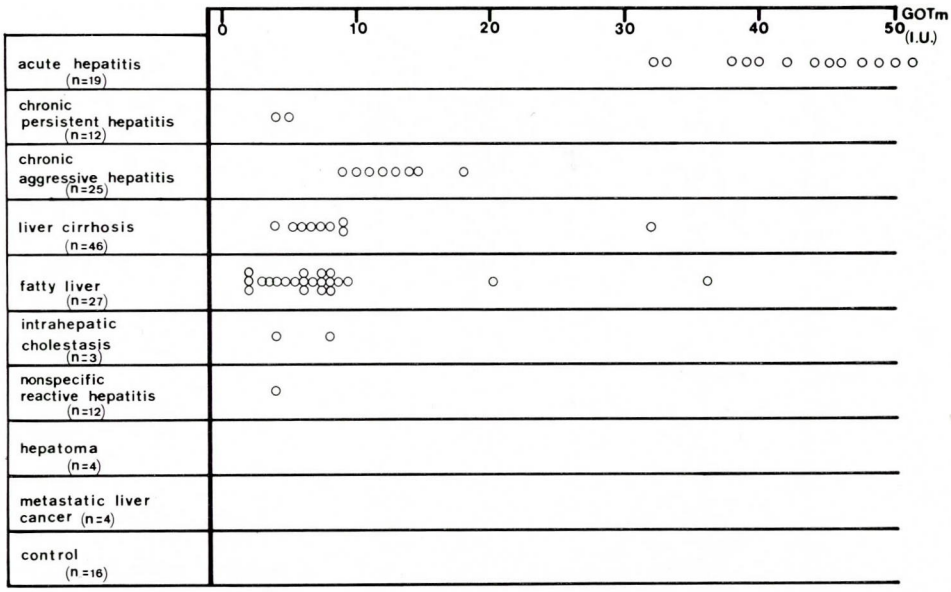
Table 1. Frequency of patients with GOT_m activity in liver diseases



(II) Activity of GOT_m in blood serum (Table 2)

In the florid stage of acute viral hepatitis, the activity of serum GOT_m was in the range of 30-40 International Units (IU), while the activity of GOT_m was slight during convalescence. In patients with chronic aggressive hepatitis, the activity of serum GOT_m was in the 10-20 IU range and in patients with the other above mentioned liver diseases, serum GOT_m activity was generally less than 10 IU, with the exception of a few cases of fatty liver and liver cirrhosis.

Table 2. Activity of serum GOT_m in liver diseases



(III) Appearance and duration of serum GOT_m activity in the clinical course of acute viral hepatitis (Fig. 1)

In Fig. 1, the appearance and duration of serum GOT_m activity are shown in relation to serum bilirubin level in the course of acute viral hepatitis. In cases of more than 10mg of total bilirubin level in blood serum, serum GOT_m activity was found at the time of admission and mostly disappeared from the blood serum by the sixth week after admission. In these patients, the highest bilirubin level in blood serum could be recognized generally in the clinical course after admission and was normalized by the 13th hospital week. In cases with less than 10mg of total bilirubin level and positive activity of GOT_m in blood serum on admission, GOT_m activity disappeared by the 4th hospital week and total bilirubin level returned to the normal range by the 8th hospital week. In Fig. 2, the correlation between GOT_m and GOT_t activity in the clinical course of a patient is shown.

(IV) Appearance and duration of serum GOT_m activity in the clinical course of chronic liver diseases

In patients in the florid stage of acute viral hepatitis and in patients with chronic aggressive hepatitis, a certain correlation between serum GOT_t and GOT_m seemed to exist, but in patients with fatty liver, serum GOT_m activity increased according to inflammatory acuity and its duration, when the fatty liver was accompanied by an inflammatory process.

In patients with the other chronic liver diseases, the appearance and duration of serum GOT_m activity showed no definite tendency but generally speaking, the rise and fall of serum GOT_m activity showed two different patterns; continuous (Figs. 3 and 4) and discontinuous (Figs. 5 and 6) appearance of serum GOT_m activity.

(V) Correlation between GOT_t and GOT_m activity in blood serum (Fig. 7)

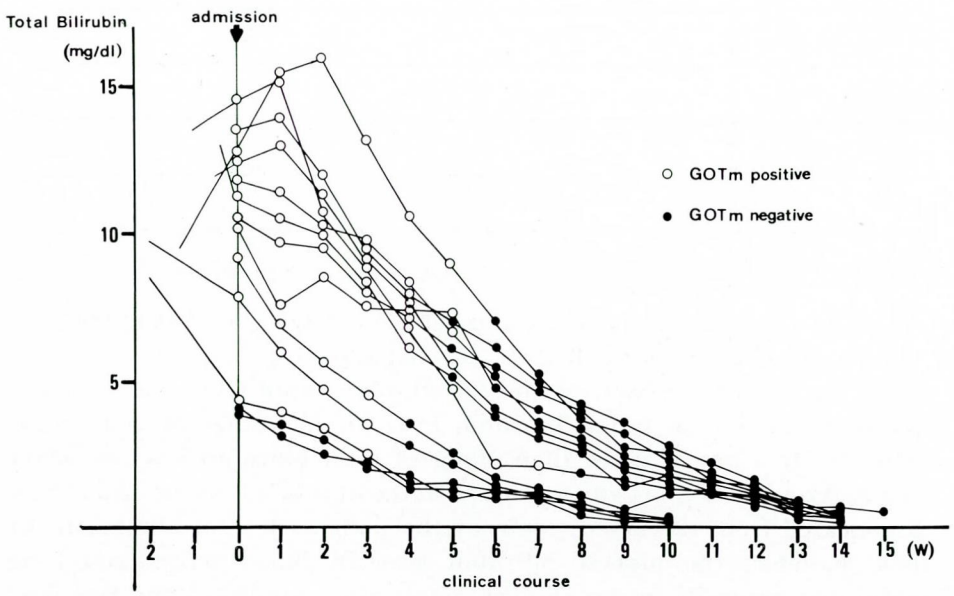
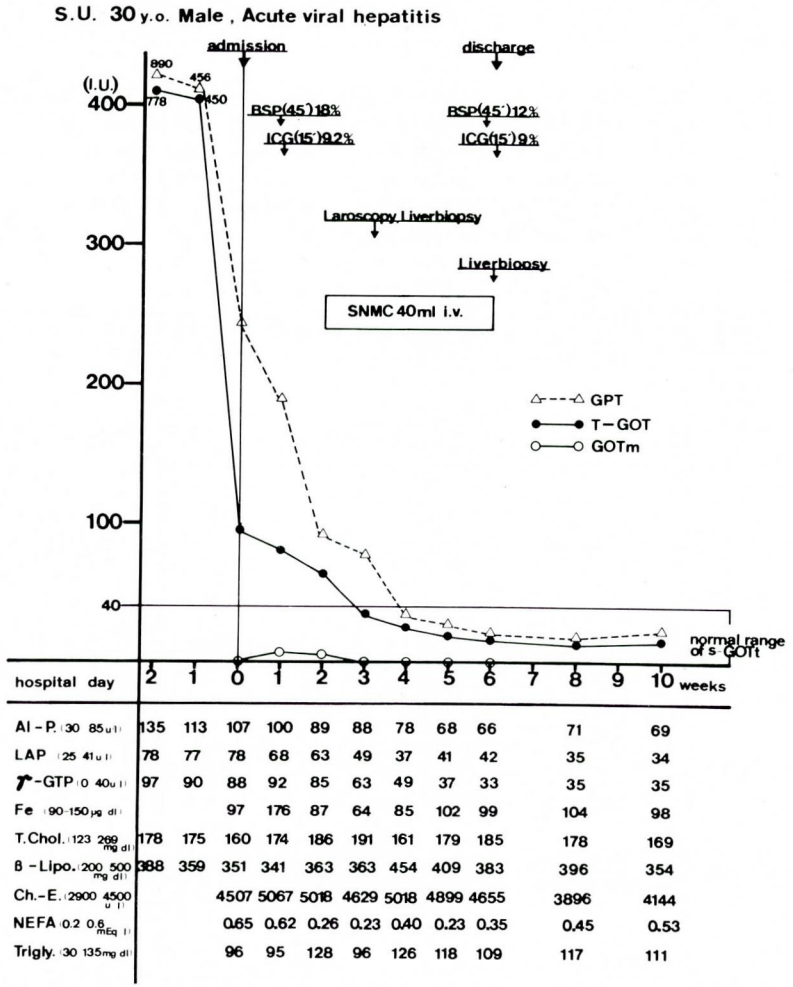
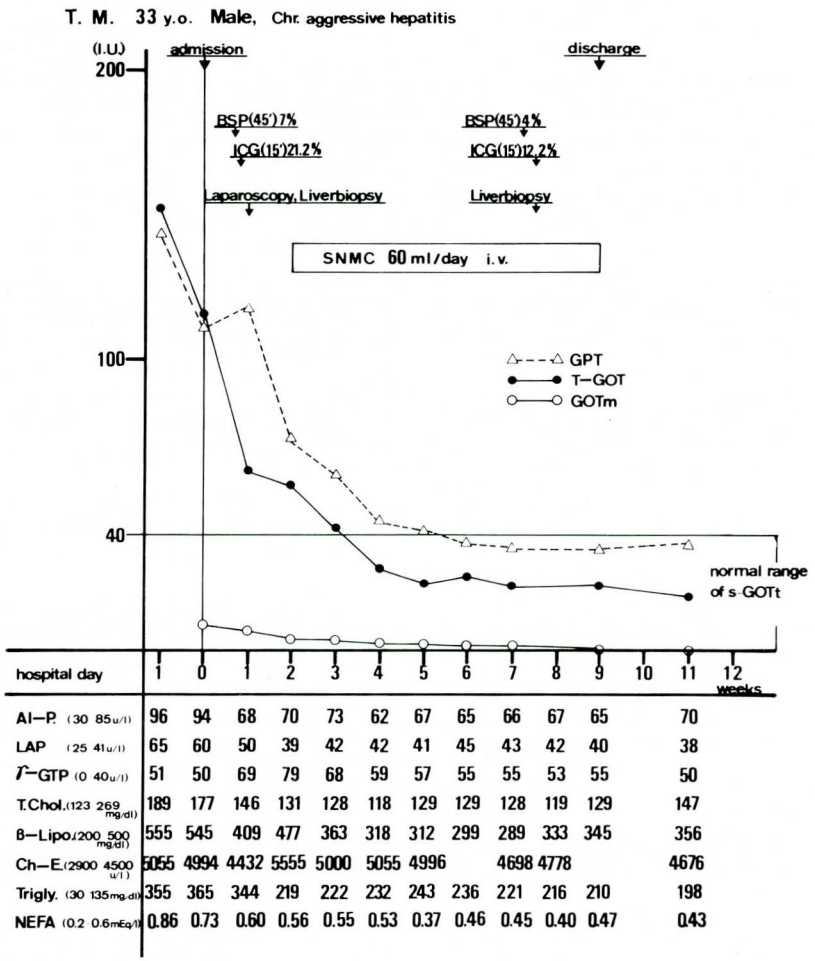


Fig. 1. Appearance and duration of positive GOT_m in relation to serum bilirubin in acute viral hepatitis



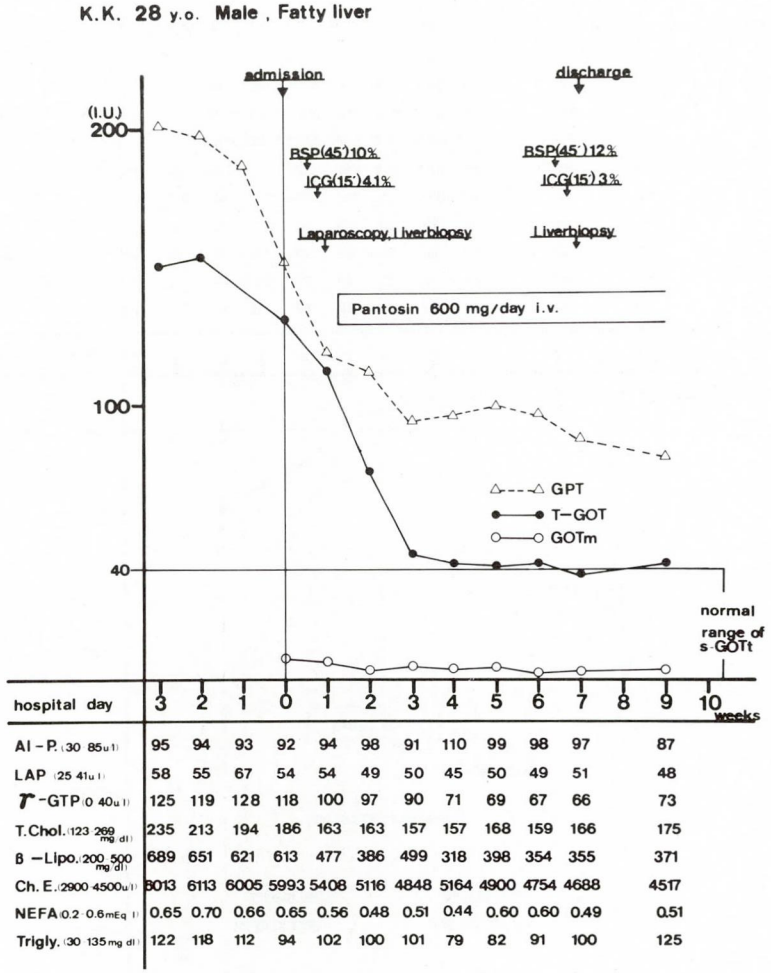
Al-P. (30 85u/l)	135	113	107	100	89	88	78	68	66	71	69
LAP (25 41u/l)	78	77	78	68	63	49	37	41	42	35	34
γ-GTP (0 40u/l)	97	90	88	92	85	63	49	37	33	35	35
Fe (90-150μg/dl)			97	176	87	64	85	102	99	104	98
T.Chol. (123 269 mg/dl)	178	175	160	174	186	191	161	179	185	178	169
β-Lipo. (200 500 mg/dl)	388	359	351	341	363	363	454	409	383	396	354
Ch.-E. (2900 4500 u/l)			4507	5067	5018	4629	5018	4899	4655	3896	4144
NEFA (0.2 0.6 mEq/l)			0.65	0.62	0.26	0.23	0.40	0.23	0.35	0.45	0.53
Trigly. (30 135mg/dl)			96	95	128	96	126	118	109	117	111

Fig. 2. The correlation of GOT_m to GOT_t activity in clinical course of a 30 year-old male (HB-positive)



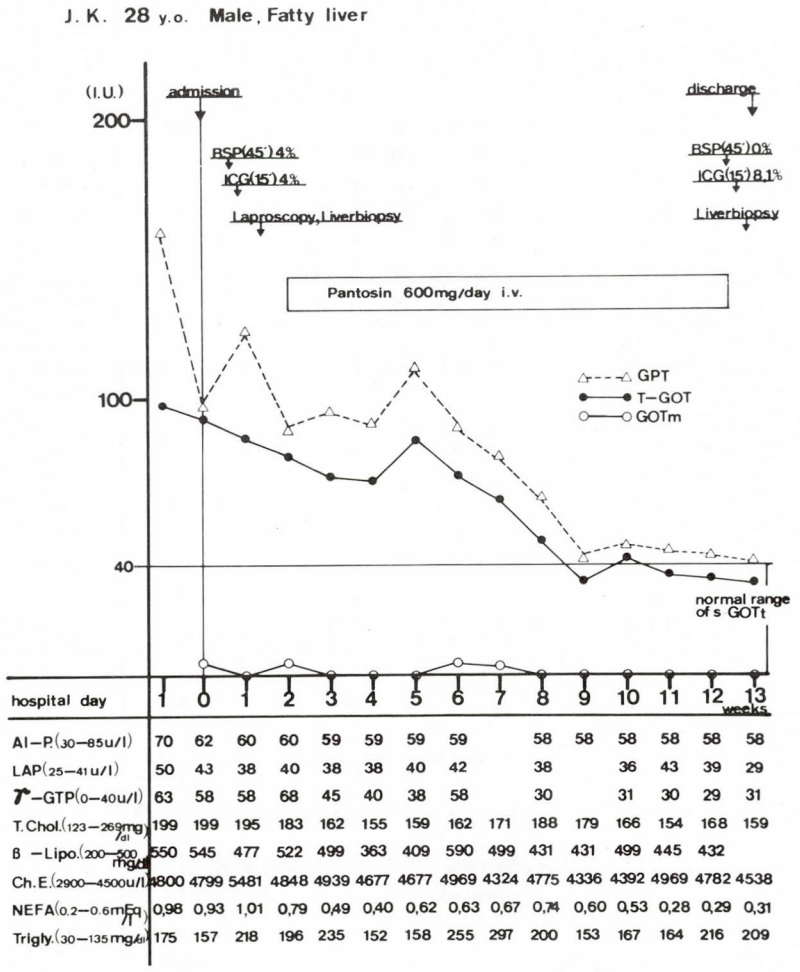
Al-P. (30 85u/l)	96	94	68	70	73	62	67	65	66	67	65	70
LAP (25 41u/l)	65	60	50	39	42	42	41	45	43	42	40	38
γ-GTP (0 40u/l)	51	50	69	79	68	59	57	55	55	53	55	50
T.Chol. (123 269 mg/dl)	189	177	146	131	128	118	129	129	128	119	129	147
β-Lipo. (200 500 mg/dl)	555	545	409	477	363	318	312	299	289	333	345	356
Ch-E. (2900 4500 u/l)	5055	4994	4432	5555	5000	5055	4996		4698	4778		4676
Trigly. (30 135mg/dl)	355	365	344	219	222	232	243	236	221	216	210	198
NEFA (0.2 0.6mEq/l)	0.86	0.73	0.60	0.56	0.55	0.53	0.37	0.46	0.45	0.40	0.47	0.43

Fig. 3



Al-P.(30 85u l)	95	94	93	92	94	98	91	110	99	98	97		87
LAP (25 41u l)	58	55	67	54	54	49	50	45	50	49	51		48
γ-GTP(0 40u l)	125	119	128	118	100	97	90	71	69	67	66		73
T.Chol.(123 269 mg/dl)	235	213	194	186	163	163	157	157	168	159	166		175
β-Lipo.(200 500 mg/dl)	689	651	621	613	477	386	499	318	398	354	355		371
Ch. E.(2900 4500u/l)	3013	6113	6005	5993	5408	5116	4848	5164	4900	4754	4688		4517
NEFA(0.2 0.6mEq l)	0.65	0.70	0.66	0.65	0.56	0.48	0.51	0.44	0.60	0.60	0.49		0.51
Trigly.(30 135mg dl)	122	118	112	94	102	100	101	79	82	91	100		125

Fig. 4. Continuous appearance of serum GOT_m activity in patient with fatty liver (28 y.o. male)



Al-P.(30–85u/l)	70	62	60	60	59	59	59	59		58	58	58	58	58	58
LAP(25–41u/l)	50	43	38	40	38	38	40	42		38		36	43	39	29
γ-GTP(0–40u/l)	63	58	58	68	45	40	38	58		30		31	30	29	31
T.Chol.(123–269mg/dl)	199	199	195	183	162	155	159	162	171	188	179	166	154	168	159
β-Lipo.(200–500 mg/dl)	550	545	477	522	499	363	409	590	499	431	431	499	445	432	
Ch.E.(2900–4500u/l)	4800	4799	5481	4848	4939	4677	4677	4969	4324	4775	4336	4392	4969	4782	4538
NEFA(0.2–0.6mEq/l)	0,98	0,93	1,01	0,79	0,49	0,40	0,62	0,63	0,67	0,74	0,60	0,53	0,28	0,29	0,31
Trigly.(30–135mg/dl)	175	157	218	196	235	152	158	255	297	200	153	167	164	216	209

Fig. 5. Discontinuous appearance of serum GOT_m activity in patient with fatty liver (28 y.o. male)

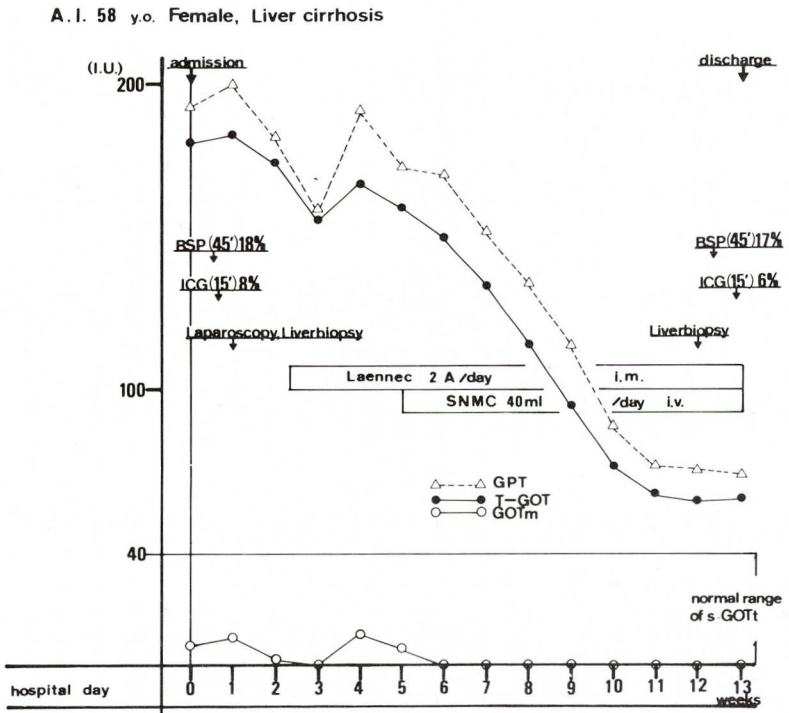


Fig. 6. Discontinuous appearance of serum GOT_m activity in patient with liver cirrhosis (28 y.o. male)

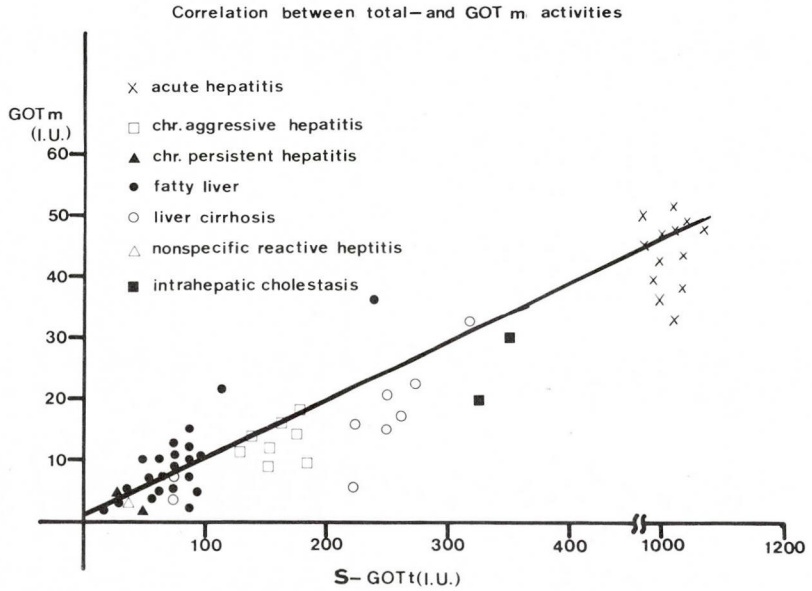


Fig. 7. Correlation between GOT_t and GOT_m activity in blood serum

DISCUSSION

At the present time, column chromatography and electrophoresis are used as routine methods in biochemical research for the separation of GOT_m and GOT_s. Since these methods require a long time for the separation of the isozymes and can not always bring about constant ratios of the isozyme recoveries, it has been stressed that separation using plate electrophoresis has some advantages over column chromatography and electropherosis (2). The authors investigated the clinical significance of serum GOT_m based on the separative assay of GOT isozyme.

Currently, it is pointed out that it is rather hard to liberate GOT_m into blood serum and that GOT_m activity can be elevated in blood serum only when the liver is severely injured. We must take the meaning of severe hepatic injury into consideration. Does severe hepatic injury not always mean fulminant hepatitis or subacute hepatitis? Because serum GOT_m activity can be found in patients in the florid stage of acute viral hepatitis and lasts mainly for the initial 4—5 weeks of the clinical course of 12 weeks after admission. The authors did encounter a small number of patients with acute viral hepatitis without serum GOT_m activity at the time of admission. Considering the clinical course, they were perhaps admitted to the author's hospital at the time of disappearance of serum GOT_m activity or immediately after disappearance of serum GOT_m activity. In other words, it can be assumed that the florid stage, in which serum GOT_m activity is elevated, had elapsed before admission. In any case, serum GOT_m activity was elevated in nearly every patient with acute viral hepatitis, at least in the florid stage (3, 4, 5). Therefore, it seems to be possible to evaluate the prognosis quod functionem et vitam of the disease based on the rise and fall of serum GOT_m activity. Further, a rapid and extensive injury of the liver, such as acute hepatitis, can bring about the liberation of GOT_m into the blood serum. On the basis of this fact, we must take the meaning of severe hepatic injury into consideration (3).

In patients with chronic aggressive hepatitis, serum GOT_m activity was found in 32% of the cases. The activity was in the 10—20 IU range and the estimated value followed the level of the floride stage of acute viral hepatitis. The rise and fall of serum GOT_m activity showed no definite correlation with the results of routine blood chemical examinations. The authors could not find any evident distinction in the results of blood chemical analyses and histological findings of the biopsied liver between negative and positive serum GOT_m groups of patients. The duration of the rise and fall of serum GOT_m activity showed two different types of continuity, continuously positive and discontinuously positive. Even in the group with the discontinuous rise and fall, serum GOT_m activity did not always show a correlation with the results of routine blood chemical examination, although several authors have pointed out that serum GOT_m activity appeared when the inflammatory process relapsed (3).

In patients with chronic persistent hepatitis and liver cirrhosis, the incidence of serum GOT_m was less than that in cases of chronic aggressive hepatitis and it can be said that the clinical significance does not differ

from that of chronic aggressive hepatitis.

In more than 80% of patients with fatty liver, serum GOT_m activity was recognized in the 2-8 IU range. As mentioned above, rapid and extensive injury of the liver, such as acute viral hepatitis, can bring about the liberation of GOT_m into blood serum. Fatty liver is a chronic diffuse degenerative change of the liver but never has a rapid extensive effects on the liver. However, serum GOT_m activity can be found in the majority of patients with fatty liver. The mechanism and clinical significance of the appearance of serum GOT_m activity can not be clarified and the fact that serum GOT_m activity can be recognized in rapid and extensive injury of the liver as well as in the diffuse and degenerative effects or the liver must be kept in mind.

In patients with primary and metastatic cancer of the liver, no serum GOT_m was found, while serum GOT_m activity has been pointed out by several authors in patients with primary and metastatic cancer of the liver.

The correlation between GOT_t and GOT_m activity in blood serum did not always show a definite tendency and it was different according to the liver disease. In patients with acute viral hepatitis, chronic aggressive hepatitis and liver cirrhosis, a correlation was shown ($R = 0.795$), but in patients with fatty liver, no definite tendency was seen unless the fatty liver was accompanied by an inflammatory process.

Based on these findings, it can be said that serum GOT_m activity can be recognized in patients with acute and chronic diseases of the liver. The mechanism of appearance of GOT_m in blood serum and the clinical significance of GOT_m remain unsolved.

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REFERENCES

1) Fleisher G, Potter C and Wakim KG: Separation of two glutamic oxaloacetic transaminases by paper electrophoresis. Proc Soc Exp. Biol Med 103: 229-231, 1960.
2) Katsunuma T, Kamiguchi H, Sase M: Separative assay method for aspartate transaminase isozyme using plate electrophoresis and diazonium salts. Tokai J Exp Clin Med 1: 235-239, 1976
3) Okuyama S, Kato Y, Funayama A et al: Clinical significance of mitochondrial GOT in serum of patients with liver diseases. Jap J Gastroenterology 73: 1163-1168, 1976.
4) Ohshiro T, Kobayashi N, Fujimoto T et al: Liver diseases and mitochondrial GOT. Acta hepatol japonica 11: 186-193, 1970.
5) Villa L, Dioguardi N, and Agostoni A: Ueber das Verhalten der mitochondrialen und cytoplasmatischen Glutamat-Oxalacetat-Transaminase (GOT) in Serum bei verschiedenen Stadien von Virushepatitis. Klin Wschr 45: 44-48, 1967.