HEPATIC FUNCTION AND STRUCTURE IN CONGESTIVE HEART FAILURE[1]

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46 cases of congestive heart failure were studied as regards hepatic structure and function. A battery of liver function tests showed hypoproteinemia and hypoalbuminemia in 6 cases, disturbed A/G ratio in 15, hyperbilirubinemia in 10, thymol turbidity above 4 units in 15, cephaline cholesterol flocculation test disturbed in 13 and raised serum alkaline phosphatase (above 13 units) in 15 cases. There was a definite statistical correlationship between the degree of heart failure and of functional impairment of liver.

Various histopathological changes noted were dilatation of central vein and sinusoids, haemorrhages in the central 1/3rd to 2/3rd of the hepatic lobules, centrilobular necrosis and irregular patchy fibrosis.

The common occurrence of cardiae cirrhosis has been discussed.

Hepatic functional impairment and structural disturbances in congestive heart failure is being recognised since the early half of the last century. Various studies have been conducted in the western countries on the post-mortem appearance (Rolleston 1912 ; Katzin, Waller and Blumgart, 1939 ; Eppinger, 1920 ; Koletsky and Barnebee, 1944 ; Gostero, and Moguel, 1947), and antimortem by liver function tests and by liver biopsy (Fishberg, 1923 ; Bernstein and Simkins. 1942 ; Chavez, Sepulveda and Ortega, 1943 : Carter and McLagan, 1946 ; Kissane and Clark, 1947 ; Sheila Sherlock, 1951). This problem assumes a special significance in India because of prevalent malnutrition and extreme common incidence of cirrhosis of liver. Only a few workers from this country (Wahi and Mathur, 1947 ; Wahi, Mathur and Tandon, 1958), have studied the incidence of disturbances of hepatic structure and function in congestive heart failure.

In view of very little work done, it was considered to study this problem in detail. In the present series, 46 cases of congestive heart failure were studied as regards hepatic structure and function. This formed a part of the study already reported under 'Blood Ammonia level in Congestive heart failure (Singh *et al.*, 1962'.

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METHODS

All patients of congestive heart failure who were admitted in the indoor wards of the Department of Medicine, Rajendra Hospital, Patiala, showed classical signs and symptoms of right sided heart failure but denied any history of liver disease in the past. The case histories were charted on a special proforma and were subjected to detailed physical, radiological and Electrocardiographic examinations.

Venous pressure was measured in the anticubital vein in lying down position by the technique described by Taylor, Thomas and Schleiter, (1930) to judge the severity of congestive heart failure. Venous psessure was taken to be abnormal when it was more than 100 mm of water as suggested by Taylor *et al.* The criteria of the degree of severity of congestive heart failure was laid down empirically. Patients with venous pressure between 100 to 200 mm of water were graded as + or mild, 201 and 300 mm as ++ or moderate, 301 and 350 as +++ or severe and above 350 mm as ++++ or very severe.

In every case, a battery of liver function tests consisting of estimation of total and differential serum proteins (King, 1951 , Thymol turbidity tests (McLagan, 1957); Cephaline Cholesterol Flocculation test (Hanger, 1939), Serum bilirubin and serum alkaline phosphatase were performed,

As regards the severity of functional impairment of the liver, classification suggested by Wahi *et al.*, (1958) was adopted because it took into consideration all the liver function tests as a whole.

Needle biopsy of the liver was performed by Vim-Silverman Needle.

The specimen was preserved in formaline and was stained with haematoxylin and eosin, Van Gieson and iron stain. The histopathological study of the biopsy tissue was graded as follows :—

i. C.V.S., (Chronic Venous Congestion) grade I showing dilatation and congestion of central vein and sinusoids.

ii. C.V.S., Grade II showing dilatation of central vein sinusoidal dilatation, haemorrhages, necrosis of hepatic cell and fatty infiltration.

iii. C.V.S., Grade III showing associated fibrosis.

RESULTS

Forty six cases of congestive heart failure of various aetiologies were studied e.g. rheumatic heart disease—21 corpulmonale-4 hypertensive heart

disease-7, ischaemic heart disease-3, pericarditis-7, congenital heart disease —1, thyrotoxicosis—1 ; and anaemia—2.

As regards severity of congestive heart failure the present series consisted of grade + severity—35 cases ; grade ++ severity--6 cases ; grade +++ severity—2 cases; grade ++++ severity—3 cases.

Liver Function tests.—The following abnormalities were observed. Serum bilirubin ranged from 0.25 mg per cent to 2.9 mg per cent with a mean average of 0.702 mg per cent (S.D.±0.44) and was of the indirect Van den Berg type. Urine showed increased urobilinogen. Hyperbilirubinemia i.e. 1 mg per cent and above was present in 10 cases (22%). There was manifest Jaundice in one case who was suffering from congestive heart failure due to tubercular pericardial effusion with tubercular pleural effusion.

Total serum protein ranged from 5.40 g per cent to 7.1 g per cent with a mean average of 6.277g per cent ((S.D ± 0.68). Hypoproteinemia i.e. below 5.49g per cent was present in 6 cases. Serum albumin level ranged from 2 72g per cent to 5.0g per cent with a mean average of 4 10g per cent (S.D. ± 0.924). Hypoalbuminemia i.e. below 3.19g per cent was present in 6 cases. Serum globulin ranged from 2.0g per cent to 2.73g per cent with amean average of 2.261g per cent (S.D. ± 0.141) and was above 2.7g per cent in 6 cases. Albumin and globulin ratio was disturbed in 15 cases.

As regards flocculation tests, thymol turbidity ranged from 2.0 units to 10 units with a mean average of 93.63 (S.D. ± 2,06). It was above 4 units in 15 cases. Cephaline cholesterol flocculation test showed more than + flocculation in 13 cases. Serum Alkaline phosphatase ranged from 3 units to 26 units with a mean average of 12.41 units (S.D. ± 5.68). It was above 13 units in 15 cases.

The liver function tests were correlated with the severity of congestive heart failure. The results are tabulated below.

Statistically correlating the severity of congestive heart failure with the various liver function tests (as given in Table II below),the coefficient of correlation gives values of 'r' which are highly significant as in each test the value of 't' is greater than 2.

TABLE I

Showing the average of results of hepatic functional tests in different degrees of congestive heart failure

Severity of congestive heart failure	No. of cases	Serum alk. phos. units/ 100 ml	Thymol turbidity units/ 100 ml	Geph. chol. floc. test	Serum bilirubin mg%	Total serum protein g%	Serum able g%	Serum glb. g%	A/G ratio
Normal.		3-13	0-3	0-+	Below 0.4	Above 5.98	Above 3.96	Below 2.21	Above 1.6
+	35	10.8*	2.91	0.4+	0.57	5.98	4.12	2.21	1.95
		4.34**	1.337		0.2306	0.4285	0.8194	0.03	0·3094.
		***(3-21)	(2-8)		(0.3-1.24)	(5.48-7.1)	(2.75-4.9)	(2.1-2.73)	(1.0 2.22)
++	6	18.0	5.56	1.83+	0.858	5.77	3.34	2.43	1.39
		4.97	3.166		0.2648	1.01	0.6255	0.2347	0.3419
		10-26	2.4-10		(0.4-1.2)	(5.42-6.8)	(2.72-4.6)	(2.2-2.7)	(1.0 2.09)
+++	2	19.5	3.3	2+	1.9	5.90	3.70	2.20	1.65
		0.5	1.3		1.0	0.3-	0.4	0.1	0.26
		(19-20)	(2-4.6)		(0.9-2.9)	5.6 6.2).	3.3 to 4.1)	2.1- 2.3)	(1.34-1.87)
++++	3	20.66	6.9	2.33+	1.20	5.506	3.06	2.44	1.25
		4.22	1.042		0.204	0.429	0.2728	2.2067	0.1936
		(15-25)	(5.5-8.0)		(1-1.5)	5.4 5.65)	(2.76-3.42)	(2.23-2.71)	(1.01 61.50).

* Mean **=S.D. ***=Range

TABLE II

Showing values of 'r' and 't' in various liver function tests

	Alk. phos.	Thymol turbidity	Serum bilirubin	Total serum prot	Serum alb	Serum glob.	A/G ratio
'r'	+0.59	+0.42	+0.41	−0.44	−0.41	+0.40	−0.39
't'	4.82	3.06	2.99	3.28	2.99	2.91	2.81

The above Table shows that relation of 'r' is direct as regards serum alkaline phosphatase, thymol turbidity, serum bilirubin and serum globulin is concerned. In the rest of the liver function tests i.e. total serum protein, serum albumin and A/G ratio, the relation of 'r' is inverse. When both the Tables (I and II) are examined together the fact that there is a significant deviation from the normal liver functions in different degrees of severity of

congestive heart failure is established. The central tendency between the various grades of severity of congestive heart failure and thymol turbidity, total serum proteins and serum albumin have not maintained the trend and this discrepancy can be explained that the number of cases is rather small for statistical analysis in grade III & IV.

Histopathological changes.—Histopathological studies were conducted by obtaining specimen of liver biopsy in 24 cases of congestive heart failure. The changes noted were as follows :—

i. Dilatation of the central veins was invariably present in all the cases. In 5 cases, the central vein was ruptured and in one case it was thickened.

ii. The sinusoids entering these veins were dilated and engorged with blood (24 cases).

iii. In three cases, there was evidence of haemorrhages in the central 1/3rd to 2/3rd of the hepatic lobules.

iv. Liver cell plates were correspondingly narrower or disorganised especially when associated with dilatation of the sinusoids. Centrilobular necrosis of varying degree was present in 13 cases associated with polymorphonuclear or round cells infiltration in varying numbers.

v. Mild to moderate fatty change was present in 5 cases, seen both in centrilobular as well as periportal zones.

vi. Non-iron staining pigment was present in the liver cells in the majority of the cases, while in a few the pigment gave positive iron staining reaction.

vii. Increased fibrosis was seen in 3 cases which was patchy and irregular in distribution.

In addition to the above changes miliary tuberculosis of the liver was present in 2 cases. Both these patients were suffering from tubercular pericardial effusion with thickened pleura and tubercular peritonitis.

The structural damage of the liver as detected by histopathological studies was analysed in relation to the degree of severity of congestive heart failure. The results are tabulated in the following table:

TABLE III

Showing the relationship between the severity of congestive heart failure and the degree of structural damage of the liver

Severity of congestive heart failure	Total No. of cases	No. of cases where biopsy was possible	Histopathological changes		
			Grade I	Grade II	Grade III
+	35	15	6	9	—
++	6	5	2	2	1
+++	2	2	—	2	—
++++	3	2	—	—	2

Though there are many overlaping figures, the above Table shows that there is a tendency for correlation between the severity of congestive heart failure and liver damage. Severe cases of congestive heart failure were more often associated with greater damage of the liver. Cardiac cirrhosis was present in two cases of congestive heart failure of +++ severity. Histopathological changes of Grade II were present in rest of the groups i.e. severity 1+, 2++& 3+++.

DISCUSSION

Hepatomegaly is a constant feature in patients of congestive heart failure due to back pressure and accumulation of blood in the liver. Liver is the only organ which is supplied predominantly by venous blood, nearly two third of the blood supply being venous in origin (MacLeod and Pearce, 1914). Therefore, liver is already in a chronic stage of hypoxia which further increases in congestive cardiac failure. It is, therefore, natural for liver functions to be impaired in patients of congestive heart failure. In the present series 15 cases of congestive heart failure showed different degrees of functional impairment.

Of the 46 cases studied, hypoproteinaemia and hypoalbuminemia was present in 6 cases, albumin globulin ratio was disturbed in 15 cases; hyperbilirubinemia was present in 10 cases; cephalin cholesterol flocculation tests showed more than + flocculation in 13 cases, Thymol turbidity existed above four units in 15 cases; serum alkaline phosphatase was raised above 13 units in 15 cases. It seems that in the present study thymol turbidity and alkaline phosphatase tests were abnormal in majority of the patients. These results are partly in conformity with those of Lichtman (1953) who observed that only serum alkaline phosphatase was one of the most sensitive mechanism to be impaired in heart failure. Sheila Sherlock (1951) however laid more emphasis on bromosulphthalein test.

To find out whether this functional impairment is due to congestive heart failure alone or as a result of some coincidental factors, e g. malnutrition, infection, etc. a correlationship between the severity of congestive heart failure and degree of functional impairment was attempted. It was observed as mentioned above that there is a definite statistical correlationship between the severity of congestive heart failure and degree of functional impairment. Etiology of congestive heart failure, however, did not have much influence on the functional impairment. Coincident malnutrition or infection probably influenced aggravation of congestive heart failure and not by directly damaging the liver.

Histophathological examination showed dilatation of central vein, sinusoids and haemorrhages as a result of rupture of the sinusoids. Central zonal necrosis was present in 13 cases. This finding has also been observed by earlier workers. (Sheila Sherlock, 1951; Wahi *et al*, 1958,. The pathogenesis of central zonal necrosis has also been discussed though not proved. Wahi *et al.*, (1958), considered the peculiarity of blood supply of liver lobules and throttling of hepatic central lobule produced by fine arborisation of hepatic vein branches. On the other hand, Sheila Sherlock (1951), attributed it to high cardiac output with low oxygen content of blood.

Cardiac cirrhosis is considered to be a rarity and is different from portal cirrhosis (Sheila Sherlock; 1951) histopathologically. Sheila Sherlock (1951), performed liver biopsy in 41 cases and observed cardiac cirrhosis to be a rarity. Wallace and Paper (1950) made a study of 200 autopsies and did not find a single case of cardiac cirrhosis. However, in the present series, 3 cases were detected to be suffering from cirrhosis out of 24 cases in which liver biopsy was attempted. Thus, greater incidence in this country has also been observed by Wahi *et al.*, (1958), who demonstrated marked cirrhosis in 5 cases, out of 29 patients. This greater incidence in this country may be explained on the basis of the fact that patients came very late for admission to the hospital. Severity of congestive heart failure may be another correlationship between the degree of hepatic structural and functional damage.

The pathogenesis of cardiac cirrhosis has been discussed by Sheila Sherlock (1951), who observed that earliest change was centrizonal reticular condensation with collapse of the reticular stroma and reticular proliferation. This was followed later on by formation of fibrous bands which result in reversed lobulation. In long standing cases cardiac cirrhosis supervened though its incidence was rare. In some instances nodular regeneration of liver cells might be seen, but it was never as conspicuous as found in portal cirrhosis.

Recognition of cardiac cirrhosis was possible in all the three cases on physical examination which was further confirmed on histopathological study. In all the three cases, ascites was out of proportion to the degree of increased venous pressure. Liver was enlarged and not tender and did not regress with treatment. Splenomegaly was not a significant finding.

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