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Role of Liv.52 and Steroids in the Management of Viral Hepatitis in Children

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INTRODUCTION

Viral hepatitis is one of the diseases which remains unconquered even in the Western countries. The incidence of the disease in advanced countries like U.S.A. is 33 per 1,00,000 population[30]. Even in our country the incidence is steadily increasing and a lot of cases are seen almost all the year round. The clinical picture shows a great variation. The disease may be inapparent or evanescent. In children its course is usually mild[9] but rarely predisposes to post-hepatitis cirrhosis, chronic cholestasis, subacute necrosis and hepatic failure.

There is so far no specific therapy for viral hepatitis, therefore it was considered desirable to ascertain the effects of Liv.52 and corticosteroids independently. A long term follow-up study was done with special emphasis on hepato-splenomegaly LFT and repeat biopsy to know the incidence of post hepatitis cirrhosis following viral hepatitis.

Liv.52 (Himalaya Drug Co. Pvt. Ltd.) is a herbal preparation and is found to have anabolic, aperient, diuretic, stomachic, haematenic and choleretic effects with protective and regenerative action on the liver and in all likelihood due to its different components. Thus it brings about definite although non-specific protective action on the liver in more than one way.

	Each tablet has processed extract of various plants	Each ml of Liv.52 drops or 2.5 ml of syrup contains:
Capparis spinosa	65 mg	17 mg
Cichorium intybus	65 mg	17 mg
Solanum nigrum	32 mg	8 mg
Cassia occidentalis	16 mg	4 mg
Terminalia arjuna	32 mg	8 mg
Achillea millefolium	16 mg	4 mg
Tamarix gallica	16 mg	4 mg
Mandur bhasma	33 mg	

The exact mode of action of Liv.52 is still not fully understood. It stimulates hepatic function probably by reducing intra-hepatic congestions, thereby relieving cholestasis. It is also likely that it helps in quicker regeneration of hepatic parenchyma.[15,18]

MATERIAL AND METHODS

A detailed study of 60 cases of viral hepatitis has been made during the period of 1971-73 in the Paediatric Wards of Niloufer Hospital with special reference of L.F.T., liver biopsy and trials with Liv.52 and prednisone. After careful detailed clinical evaluation as per detailed proforma, urine

examination for bile and liver function tests were done on the day of admission. Later on blood was sent for haemogram, blood grouping and bleeding and coagulation time prior to biopsy. Liver biopsies were done initially in 47 cases with aseptic precautions under the cover of injection of Vitamin K.

Sixty cases of viral hepatitis were randomised into four groups: A, B, C and D. All patients were given routine supportive treatment like glucose, vitamins and rest in bed. The present trial on Liv.52 has been carried out on 31 cases of viral hepatitis (Group 'A'). In Group 'B', 11 cases received supportive treatment as well as prednisone; Group 'C'–5 cases received a combination of drugs, steroids and Liv.52; Group 'D'-13 cases received only supportive treatment.

During the hospital stay, day-to-day progress was observed and after discharge, follow-up at weekly intervals, later at monthly intervals or whenever possible, was done in the Outpatient Department. Repeat biopsies were done in 15 cases after 3 to 12 weeks. A few cases were followed up even after a year.

OBSERVATIONS

Hospital statistics: Analysis of admissions, into the paediatric wards of the Niloufer Hospital during the years 1970 to 1972 is presented in Table I.

Table I: Shows the incidence, sex and mortality of cases of viral hepatitis during the years 1970-1972

Year	Total admissions	Total cases of viral hepatitis	Sex		Mortality
			Male	Female	
1970	9699	73	45	28	2
1971	9261	58	40	18	5
1972	9379	109	65	44	8

A higher incidence of viral hepatitis has been noticed during the pre-school period in the present series (Table II).

Table II: Shows age incidence of viral hepatitis at Niloufer Hospital and compared with the present series

	Hospital Statistics		Present Series	
Age	No. of cases	%	No. of cases	%
Less than 1 year	16	6.7	–	–
1–2 years	63	26.25	19	31.7
3–5 years	105	43.75	27	45.0
More than 5 years	56	23.3	14	23.3

The sex difference is not significant though in the worked out cases a higher incidence was observed in males.

Table III: Illustrates the sex incidence in the present series

Sex	No. of cases	%
Male	34	56.7
Female	26	43.3

Jaundice was observed in all cases but detected after admission in 5% of the present series. The average duration of jaundice prior to admission was 10 days but varied from 1-60 days.

Table IV: Showing duration of jaundice prior to admission		
Duration	No. of cases	%
Less than 1 week	31	51.7
1–2 weeks	9	15.0
2–3 weeks	9	15.0
3–6 weeks	6	10.0
More than 6 weeks	2	3.0
Jaundice detected after admission	4	5.0

Table V: Illustrates the seasonal incidence of viral hepatitis				
Month	No. of cases in hospital statistics	%	No. of cases in present series	%
January	21	8.7	3	5.0
February	16	6.6	4	6.6
March	19	7.9	1	1.6
April	19	7.9	5	8.3
May	14	5.8	3	5.0
June	22	9.1	8	13.3
July	14	5.8	1	1.6
August	37	15.4	9	15.0
September	21	8.7	9	15.0
October	18	7.5	5	8.3
November	24	10.0	8	13.3
December	17	7.0	4	6.6

In the present series a higher incidence was observed during late summer and winter months.

In the present series jaundice was observed in all cases and the depth of jaundice could be well correlated with the serum bilirubin levels though not with the histological lesion.

Table VI: Reveals the frequency of symptoms of viral hepatitis in the present series		
Symptoms	No. of cases	%
Jaundice and yellow discoloration of urine	60	100
Fever	55	91.6
Asthenia	45	75.0
Anorexia	42	70.0
Clay coloured stools	34	56.0
Vomiting	28	47.0
Diarrhoea	27	46.0
Nausea	20	33.0
Pain in abdomen	18	30.0
Respiratory tract infection	14	23.3
Headache	13	21.6
Chills and rigors	7	11.0
Pruritus	5	8.0
Insomnia	5	8.0
Altered sensorium	1	1.6
Bleeding tendencies	1	1.6

Table VII: Shows the degree of jaundice as judged clinically in the present series		
Degree of jaundice	No. of cases	%
Mild	48	80.0
Moderate	11	18.3
Severe	1	1.7

Table VIII: Illustrates the frequency of signs of viral hepatitis in the present series

Signs	No. of cases	%
Icterus	60	100.0
Hepatomegaly	59	98.0
Tender liver	31	51.0
Splenomegaly	21	35.0
Lymph node enlargement	21	35.0
Oedema Legs	4	6.0
Ascites	1	1.6
Bradycardia	1	1.6

Hepatomegaly was observed in 98% of the present series. Only in a single case it was not palpable though histopathological examination of the liver biopsy specimen revealed viral hepatitis.

Table IX: Illustrates the size of the liver in the present series		
Palpable in midclavicular line in cm	No. of cases	%
1 cm	5	8.3
2–4 cm	41	68.3
5–6 cm	9	15.0
Not certain	4	6.7
No liver enlargement	1	1.7

The serum bilirubin level could be well correlated clinically with the depth of jaundice, there was no correlation between it and the histologic lesion.

It has been observed that 23% of the present series had normal SGOT and SGPT levels in spite of elevated serum bilirubin levels. On the other hand 12% of cases showing hepatic damage on histopathological examination had normal SGOT and SGPT values.

Though the initial levels of alkaline phosphatase were normal all the cases registered a fall in the levels 15 days after treatment.

Thymol turbidity values ranged from 3.8 to 10 units in the present series. After 15 days of treatment all cases showed normal values.

Table X: Shows the serum bilirubin levels in the present series on admission				
Serum bilirubin mg%	Group 'A'	Group 'B'	Group 'C'	Group 'D'
	Liv.52 %	Prednisone %	Liv.52 + Pred. %	Supportive %
0–5	98.7	60	60	84.6
5–10	10.3	30	40	15.4
10–15	–	10	–	–

Table XI: Shows the serum bilirubin levels 15 days after treatment with Liv.52, prednisone, both and routine supportive therapy (placebo)				
Serum bilirubin mg%	Group 'A'	Group 'B'	Group 'C'	Group 'D'
	Liv.52	Prednisone	Liv.52 + Prednisone	Supportive therapy
0–1	13.8	–	–	23.1
1–2	82.8	90	60	61.5
2–3	3.4	10	20	–
3–5	–	–	–	15.4
More than 5	–	–	20	–

Table XII: Shows improvement in biochemical tests 15 days after treatment

Biochemical test	Group 'A'	Group 'B'	Group 'C'	Group 'D'
	Liv.52 %	Prednisone %	Liv.52 + Pred. %	Supportive therapy %
1. Bilirubin fall to less than 2 mg	96.6	90.0	66.6	84.6
2. Fall of SGOT to 40 units and below	89.4	77.7	75.0	81.8
3. Fall of SGPT to 40 units and below	85.7	55.5	–	72.7

Table XIII: Illustrates serum alkaline phosphatase levels on admission (a) and 15 days after treatment (d)

Serum alkaline phosphatase levels	Group 'A' % Liv.52		Group 'B' % Prednisone		Group 'C' % Liv.52 + Pred.		Group 'D' % Supportive	
	(a)	(d)	(a)	(d)	(a)	(d)	(a)	(d)
10–15	26.1	52.2	12.5	100	25	50	33.3	83.3
15–20	69.6	47.8	75.0	–	50	50	66.7	16.7
20–25	4.3	–	12.5	–	25	–	–	–

(a) — On admission; (b) — 15 days later.

Table XIV: Shows thymol turbidity levels of the present series at the time of admission (a) and 15 days after treatment (d)

Thymol turbidity test units/ml	Group 'A' % Liv.52		Group 'B' % Prednisone		Group 'C' % Liv.52 + Pred.		Group 'D' % Supportive	
	(a)	(d)	(a)	(d)	(a)	(d)	(a)	(d)
0–5	91.7	100	85.7	100	100	100	89.2	100
5–10	8.3	–	14.3	–	–	–	30.8	–

Table XV: Shows rise in proteins 2–4 weeks after treatment

Rise in proteins in g%	Group 'A' Liv.52	Group 'B' Prednisone	Group 'C' Liv.52 + Pred.	Group 'D' Supportive
0.1–0.5 g	43.5	–	–	11.1
0.5–1g	39.1	57.1	66.7	44.4
Stationary	8.7	14.3	–	22.2
Fall	8.7	28.6	33.3	22.2

Histopathological Studies of the Liver Biopsy Material

In the present study liver biopsy was done for 47 out of 60 cases and repeat biopsy for 15 cases. Initially all cases showed vacuolation of varying degrees of hepatocytes with scanty and granular cytoplasm. The portal tracts were infiltrated with mononuclear cells and segmented leucocytes. The lobular parenchyma was found as muralium duplex in all cases.

In most of the cases biliary canaliculi and Kupffer cells were prominent. Focal areas of liver cell necrosis were noted in few of them. The limiting plate was destroyed in some of them. Cholestasis was appreciable only occasionally and in such cases bile pigment could be seen in hepatocytes and also in biliary canaliculi. By and large the glycogen content of the liver cells was found to be reduced in sections stained with PAS. A striking feature was an intact lobular architecture in all cases. The reticulin framework was not disturbed.

Table XVI: Shows the repeat biopsy studies

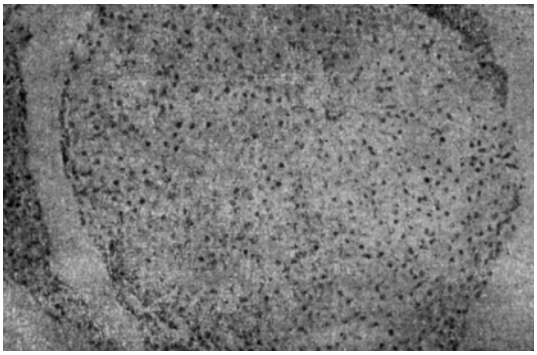
Group	Case No.	Particulars
A Liv.52	2	Second biopsy after 6 weeks showed incomplete recovery but third biopsy after 4 months revealed complete recovery.
A Liv.52	3	Second biopsy after 6 weeks revealed persistence of the lesion but third biopsy after 1 year showed normal architecture of the liver.
A Liv.52	4	Second biopsy after 6 weeks showed complete recovery. Third and fourth biopsies repeated after 8 and 10 months also showed normal architecture of the liver.
A Liv.52	7	Second biopsy after 3 weeks showed only minimal vacuolation of the cells and mononuclear infiltration of the portal tracts. Third biopsy repeated after 3 months and

		fourth biopsy 1 year 9 months later both revealed normal architecture of the liver.
A Liv.52	11	Repeat biopsy after 4 weeks revealed only minimal vacuolation of the hepatocytes. Otherwise essentially negative.
A Liv.52	13	Repeat biopsy after 3 weeks showed minimal mononuclear infiltration within the portal tracts.
A Liv.52	29	Repeat biopsy after 3 months revealed normal architecture of the liver.
A Liv.52	10	Incomplete recovery after 1 month.
B Prednisone	27	Repeat biopsy after 8 weeks revealed persistence of mononuclear infiltration of the portal tracts vacuolation of hepatocytes and focal areas of liver cell necrosis.
B Prednisone	28	Repeat biopsy after 6 weeks showed persistence of mononuclear infiltration, vacuolation of liver cells and fibroblastic reaction.
C Liv.52 + Prednisone	9	Repeat biopsy after 4 weeks showed persistence of activity of the lesion.
C Liv.52 + Prednisone	23	Liver was essentially negative even at the time of admission though clinical and biochemical findings were strongly suggestive of viral hepatitis —repeat biopsy also revealed normal liver.
D Supportive	39	Repeat biopsy after 9 months revealed persistence of the activity of the lesion.
D Supportive	49	Repeat biopsy after 4 weeks revealed persistence of the activity of the lesion.
D Supportive	57	Repeat biopsy after 8 weeks revealed incomplete recovery of the histological lesion.

DISCUSSION

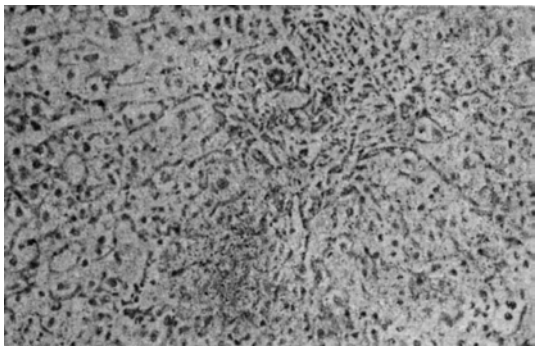
Out of 28339 cases admitted in the children's ward of Niloufer Hospital, for the years 1970-72 there were 240 cases of viral hepatitis thus accounting for 0.7% of the total admissions with a mortality of 6%. The incidence according to Viswanathan *et al* is 1.2%[27]. The reasons for the higher incidence reported by other authors may be that only moderate to severe cases are admitted in hospital. Further, there is a higher incidence of anicteric cases in children which have not been included in the statistics. It should be remembered that in children one case of icteric viral hepatitis represents 12 cases of the anicteric type (Krugman 1962)[10]. Though it has been mentioned that viral hepatitis is often a self limiting disease mortality is high during epidemics[16] and even higher in adults.

In the present study, patients ranged from 1–12 years. A higher incidence has been noticed during the pre-school period in the present series, as also by Dave *et al*[3]. But a higher incidence during the school age was observed by Nelson and Deshpande *et al*[4]. A higher incidence was noticed during the late summer and winter months, which agrees with the observations of other workers[27].

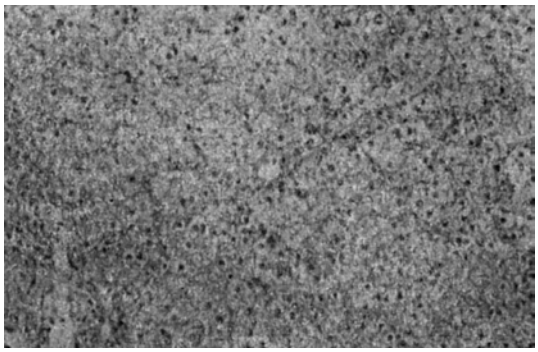


Normal liver cell pattern *L.P.* 10 x 10

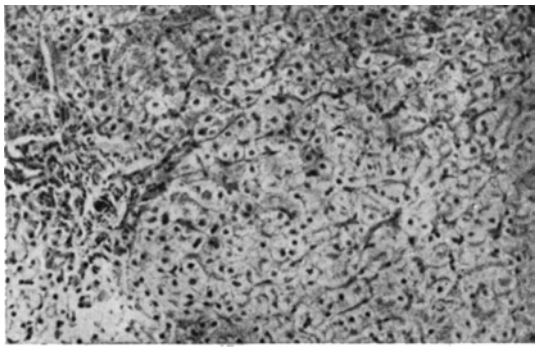
TYPICAL PRE-TREATMENT MICROPHOTOGRAPHS



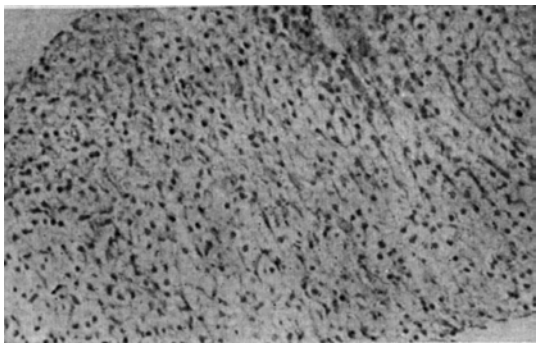
Infiltration of the portal tract by mononuclear cells and leucocytes *L.P.* 10 x 10



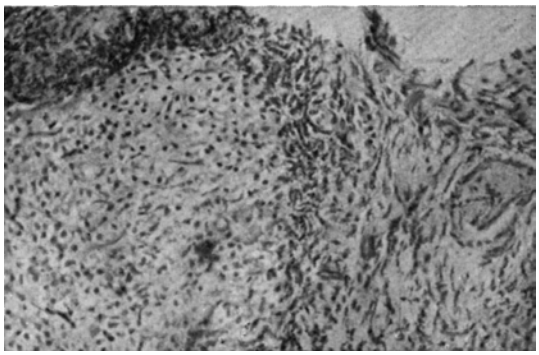
Ballooning of the hepatocytes *L.P.* 10 x 10



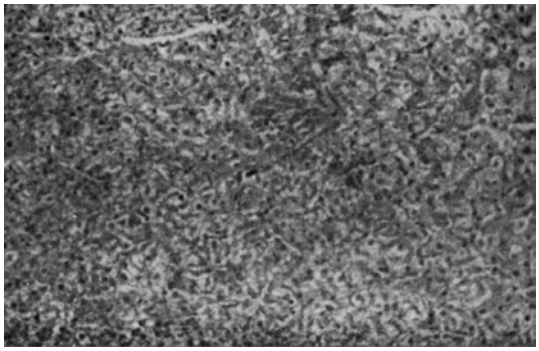
Case No. 29 (Group A – Liv.52)
Initial Biopsy showing infiltration of the portal tract by mononuclear cells. *L.P.* 10 x 10



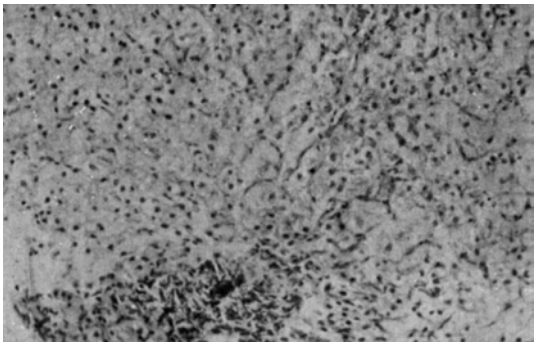
Case No. 29 (Group A – Liv.52)
Repeat Biopsy showing recovery.
L.P. 10 x 10



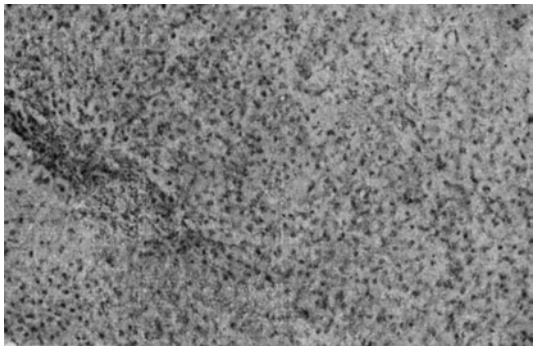
Case No. 3 (Group A – Liv.52)
Initial Biopsy showing mononuclear infiltration of the portal tracts. *H.P.* 10 x 10



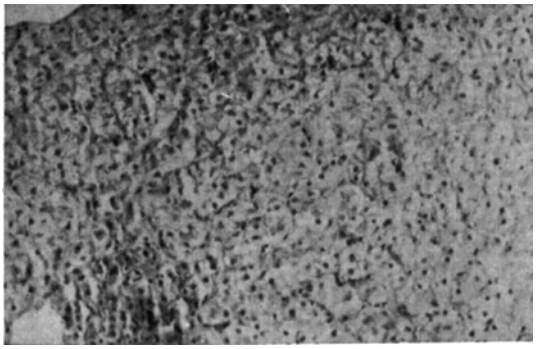
Case No. 3 (Group A – Liv.52)
Repeat Biopsy shows recovery.
L.P. 10 x 10



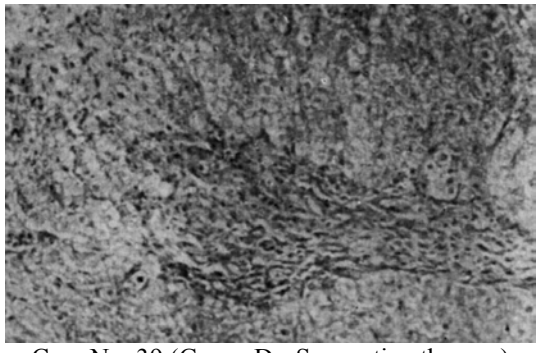
Case No. 27 (Group B – Prednisone)
Initial Biopsy showing periportal infiltration.
L.P. 10 x 10



Case No. 27 (Group B – Prednisone)
Repeat Biopsy showing perisistence of the lesion. *L.P.* 10 x 10



Case No. 39 (Group D - Supportive therapy)
Initial Biopsy showing fibroblastic reaction mononuclear infiltration of the portal tracts.
L.P. 10 x 10



Case No. 39 (Group D - Supportive therapy)
Repeat Biopsy showing persistence of the lesion.
L.P. 10 x 10

Eighty five per cent of the present series belonged to poor socio-economic status and 15% to the middle income group. This is attributed to poor sanitation and bad personal hygiene in these groups. History of contact was obtained in about 16% of cases. Absence of this history in other cases is probably due to the occurrence of anicteric cases and mild jaundice which may not be noticed due to ignorance. In the present series the illness was of sudden onset in 63% and insidious in 37% of cases. The mode of onset has been described by Mallory[14] and Lichtman[12] as follows: (1) acute infectious type (2) gastrointestinal type (3) mixed (4) cerebral symptoms. The most frequent prodromal symptoms in the present series were gastro-intestinal (46%), respiratory symptoms (23%). About 6% of the cases were brought with neuropsychiatric symptoms and the rest with constitutional symptoms.

In India, 90% of jaundice is due to viral hepatitis[3]. This was observed in all cases of the present series but in 5% it could be detected only after admission. Table 6 shows the duration of jaundice prior to admission, the average being 10 days. Jaundice was preceded by a history of passing highly coloured urine 1–8 days before, in most of the cases. Pyrexia was noted in 91.6% of the present series, but it continued into the icteric stage only in about 45% of the cases. Lichtman attributes fever to necrosis of hepatic cells, secondary infection of bile channels and necrotic foci, and enteritis with lymphangitic infection of the mesentery[12]. Weakness and fatiguability was noticed in 75% of the cases. Asthenia was attributed to disturbed myoneural physiology by retained bile salts; a disturbance in carbohydrate metabolsim which leads to delayed conversion of lactic acid to glycogen stores and to vitamin E deficiency due to lack of absorption[12]. Anorexia is one of the presenting features of viral hepatitis (Sherlock)[24]. This was observed in 70% of the present series and 40% as observed by Sule *et al*[26]. The average duration of anorexia prior to admission was 16

days but varied from 2–60 days. Infants refused feeds. Anorexia was more marked for fatty foods in older children. The return of appetite is an index of recovery.

Vomiting was observed in 47% of the cases and nausea in 33% of the series. These were related to food in most of the cases and more prominent during the prodromal stage. Diarrhoea was encountered in 46% of the present series and 20% had diarrhoea associated with vomiting. A single case was admitted only for gastroenteritis and jaundice could be detected only on the day after admission. Diarrhoea is attributed to the presence of intestinal cattarrh and is common in children, though according to Nelson constipation is more common than diarrhoea[17]. Constipation was encountered in 5% of the cases only. This is more often seen in adults. The history of passing clay coloured stools was obtained in about 56% of the present series and suggests the obstructive phase of viral hepatitis due to ballooning of the hepatocytes.

Abdominal pain was noticed in 30% which is in agreement with Sule *et al*[26]. Abdominal pain varied from mild discomfort to an acute episode suggesting a surgical problem. A single case was admitted for acute pain in the abdomen and conservative line of treatment was given. Two days later jaundice appeared. The abdominal pain could be attributed to perihepatitis, distension of Glisson's capsule, phlegmonous enteritis causing diffuse pain or sudden shrinkage of the liver in acute hepatic necrosis[12].

Mild respiratory tract infection was seen in 23.3% of the present series. Report of Lucke[13] and Mallory[14] give respiratory infections in 75% in the paediatric age group. Headache was encountered in 21.6% of the present series and 33% in Haven's series. This is most probably a constitutional symptom. In one series certain neuropsychiatric symptoms were seen. One case which was in a precomatose state became boisterous and a day later became drowsy. Three per cent of the present series had excessive sleepiness and drowsiness.

Physical Signs

Jaundice, observed in all cases, is attributed to the lack of function of hepatic parenchymal cells, obstruction of biliary canaliculi by bile thrombi, increased permeability of the smaller bile ducts and canaliculi for bile, or shortened life span of RBC. As the jaundice was clearing serum bilirubin levels also came down. Only a few cases showed persistence of serum bilirubin levels even after the jaundice cleared clinically. Clearance of jaundice varied from case to case. Hepatomegaly was the next important physical sign observed in 98.3% of the present series, 100% according to Dave *et al*[3], and 95% of Deshpande's series[4]. Only one case did not have a palpable liver though the histologic lesion was suggestive of viral hepatitis. Tenderness could be elicited only in 54% of the cases. Though Rappaport[20] concluded that the degree of hepatic tenderness varies inversely with the extent of liver enlargement, such relationship could not be elicited in the present series. Liver remained palpable for a variable time, it receded as early as 6 days in few; whereas it persisted for more than a year in 2 cases. Splenomegaly was noticed in 35% of the present series, and 20% according to Sherlock[24]. The size varied from 1-3 cm below the costal margin and it denotes a slight rise in portal pressure resulting in congestion of spleen. In most of the cases it disappeared within 1–4 weeks and occasionally persisted even after a year. Lymphadenopathy was observed in 35% of the cases. Wood[29] and Barker[1] reported a generalised lymphadenopathy in almost all of their cases. Posterior cervical lymphadenopathy on the right side was stressed by Sherlock[24], as the lymphatics draining the diaphragm are connected to them. In the present series cervical and submandibular groups were palpable, discrete, firm and not tender. Bradycardia was observed only in one case. It is more frequent in adults due to the effect of bile salts on the vagal nerve endings. The infrequency of this sign in children is probably because of sympathetic ovetonus. Ascites was also observed in a single case which completely disappeared after prednisone therapy. Ascites when present denotes a rise in portal pressure but is a rare feature[17]. Skin manifestation appeared in none of the series.

Fifteen per cent of the present series showed various manifestations of protein and vitamin deficiencies. Similar were the findings of Sheth *et al*[4]. Convalescence was quick and short in almost all cases.

Laboratory Tests

Urine examination was done on the day of admission for bile salts, bile pigments and urobilinogen. Colour of the urine varied from light yellow to dark red or port wine colour. The urine gave a positive test in almost all cases for bile pigments except in 6% where bilirubin levels were very low (less than 1.6 mg). Methylene blue test and Fouchet's test (Harrison Spot) were done in all cases but methylene blue test was found to be unreliable. In 80% of the cases urobilinogen as tested by Ehrlich's aldehyde reagent was present. Disappearance of urobilinogen signifies complete obstruction. In the present series disappearance of urobilinogen was not associated with high alkaline phosphatase levels and passing clay coloured stools in most of the cases.

Haematological Investigations

The blood counts were normal in 69%, leucopenia which is said to be characteristic was observed only in 11% of cases; leucocytosis in 20% and relative lymphocytosis in 10% of the present series. A high relative lymphocytes was recorded in 87% of cases by Finks and Blumberg.

Liver Function Tests (LFT)

Depth of jaundice could be well correlated with serum bilirubin level. In the present series 2 cases who had very low serum bilirubin levels of 1.4 and 1.7 mg% showed typical histologic lesion. One case having very high serum bilirubin level showed almost normal structure of the liver on needle biopsy of the liver therefore serum bilirubin level is not useful for prognostic purposes as it does not indicate the degree of hepatic damage[19]. Return of serum bilirubin to normal was slower when compared to SGOT and SGPT levels. Tables XI and XII illustrate the efficacy of Liv.52 and steroids in lowering hyper bilirubinemia to 2 mg% or less, within 15 days of treatment. The efficacy of Liv.52 was observed by Raju *et al*[21] and Sule *et al*[26], and that of steroids by Ducci, and Katz[6]. In the Van den Bergh reaction, a direct positive reaction was noted in most of the cases and a delayed positive was noted only in a few cases who had very low serum bilirubin levels. Thymol turbidity values ranged from 3.8 to 6 units/ml. Thymol turbidity values returned to normal at the time of discharge as illustrated in Table XIV for all cases. These tests depend on high beta and gamma globulins or a fall in albumin level. This test is considered valuable by Sherlock in detecting hepatic damage but such correlation could not be made in the present study. Serum alkaline phosphatase is a valuable test to differentiate obstructive and non-obstructive types of jaundice. Though the initial levels were normal, all the cases registered a fall in the levels 15 days after treatment (Table XIII). Ester component of total serum cholesterol may be very much reduced in hepatocellular damage. A rising cholesterolemia with declining bilirubinemia is definite evidence of convalescence. Since the method of estimating cholesterol esters is time consuming, they have a limited practical application. The values of serum proteins ranged from 3 g. to 6.4 g. in the present series. A definite rise in total serum proteins especially in those in whom the levels were low at the time of admission was observed as illustrated in Table XV at the time of discharge. Histopathological changes in liver biopsy studies varied from case to case depending upon the stage of the disease. The histopathological changes on serial liver biopsies which are reported are of different opinions[25,2,22,23,6,5]. In the present study vacuolation was noted in all cases. Portal tracts were infiltrated with mono-nuclear and segmented leucocytes. Cholestasis was appreciable only occasional. Lobular architecture was intact in all cases and the reticulin framework was not distorted.

Correlation between Clinical, Biochemical and Histopathological Changes

There was no correlation between clinical, biochemical and histopathological lesions as has been observed in the present study. In one case though the child had severe jaundice, histopathological changes were minimal and in another case the child had all clinical and biochemical features suggestive of acute viral hepatitis but histopathological examination was essentially negative. About 12% of the present series who had normal SGOT, SGPT values exhibited hepatic damage on histologic examination. Serum bilirubin levels also were not helpful in indicating the degree of hepatic damage. Presence of bile thrombi histologically may not always be associated with clinical and biochemical evidence of the obstructive phase. According to Shetana[25] these bile thrombi indicate subsiding phase of viral hepatitis. Till recently treatment has had little effect in altering the course of an ordinary case of acute viral hepatitis. Till today various drugs have been tried as therapeutic measures and various authors have claimed beneficial results (Sherlock).

Liv.52 therapy: In the present series Liv.52 was tried on 31 cases (Group 'A'). Improvement in symptomatology was observed in all cases, but earlier in the Liv.52 group. Patients experienced a subjective sense of well-being and improved as in Group B (Prednisone). Hyperbilirubinemia which is an index of severity of jaundice remarkably regressed as shown in Tables X and XI. Serial transaminase estimation also showed a considerable fall 15 days after Liv.52 therapy as illustrated in Table XI. This proved the efficacy of Liv.52[26,3,21]. Serial needle biopsy of the liver revealed a dramatic recovery of the histological lesion as also observed by Mukerjee *et al*[15, 18], the earliest improvement being 6 weeks after treatment. This was not observed in group B (Prednisone) and group D (vitamins B-complex and C). None of the cases treated with Liv.52 showed any untoward toxic symptoms and in none did jaundice recur.

Corticosteroid therapy: The observations made in the present series were in agreement with some authors i.e. steroids showed a good clinical as well as biochemical improvement[6,7,8]. (Though a single case showed fluctuation of serum bilirubin level while it was being tapered off) but the histological lesion showed little alteration[26,28]. Almost all cases of groups B and C receiving prednisone developed puffiness of the face and oedema of the feet following steroid therapy as observed by Libov[11].

Follow-up study

In Group 'A' treated with Liv.52, though almost all 31 cases came for initial follow-up study 1–2 weeks after discharge, repeat biopsy could be done only for 8 cases, 6–12 weeks after the first biopsy. Biopsy was repeated again after 1 year for 2 cases and 2 years later for one case. Most of them showed a definite histopathologcial improvement after 6–12 weeks with complete recovery in three of them and remained normal even after 1–2 years. For one case fibrosis was observed initially but repeat biopsy after 1 year revealed normal architecture of the liver.

In Group 'B' treated with prednisone, though definite clinical and biochemical responses were noted with steroids, histopathological changes were not significantly altered when compared to Group 'A'. Repeat biopsy could be done for two cases and histologic examination revealed incomplete recovery after 6-8 weeks.

In Group 'C', steroids + Liv.52, only two cases could be followed-up. One case did not have any histologic lesion even at the time of admission. Repeat biopsy after 4 weeks showed incomplete recovery for the other case.

DOSAGE SCHEDULE

Age in years	Group 'A' Liv.52	Group 'B' Prednisone	Group 'C' Liv.52 + Prednisone	Group 'D' Supportive
1–2	Liv.52 2 tsf. b.d.	Prednisone 2mg/kg	Liv.52 + Prednisone	Tab. B.C. 1 b.d. Tab. Vit. C. 1 b.d.
2–5	Liv.52 2 tsf. t.i.d	For 2 wks 1 mg/wk		
5–10	Liv.52 2 tsf. t.i.d.	For 1 wk ½ mg/kg/wk		
10–12	Liv.52 2 tabs. t.i.d.			

Since viral hepatitis is often a self limiting disease, a definite improvement in symptomatology restoration of liver function tests to normal have been observed even in Group 'D' with supportive treatment, though delayed. Three cases could be followed-up. Repeat biopsy done 4–8 weeks after the initial biopsy for 2 cases, showed incomplete recovery. Another case came for follow-up after 9 months and biopsy was repeated. Histopathological examination revealed persistence of spotty necrosis and fibroblastic reaction denoting incomplete recovery (see Table XVI).

CONCLUSIONS

Though the number of cases studied is small to draw definite conclusions, the following observations can be made:

1. Viral hepatitis is a common paediatric problem, incidence being high during late summer and winter.
2. The pre-school age group is more affected.
3. A fairly high incidence of diarrhoea and respiratory infection is observed.
4. A triad of symptoms anorexia, fever and jaundice is usually present.
5. Sixty cases were divided into 4 groups. Group 'A' was on Liv.52 alone, Group 'B' on prednisone, Group 'C' on Liv.52 + prednisone, Group D on multivitamin tablets.
6. All cases recovered completely though recovery was earlier in the Liv.52 treated cases. There were no side effects encountered with Liv.52 therapy.
7. Tender hepatomegaly was observed only in 54% of the cases, and hepatomegaly was absent in 1.6%.
8. Clearance of jaundice could be correlated well to declining hyperbilirubinemia.
9. Return of SGOT and SGPT to normal was earlier than serum bilirubin.
10. No correlation could be made between serum bilirubin and SGOT and SGPT values to histologic lesion in 23% of cases.
11. Histopathological changes were not significantly altered with steroid therapy whereas with Liv.52 histopathological recovery was dramatic.

SUMMARY

A two year study of 60 cases of viral hepatitis was undertaken.

Detailed clinical and laboratory studies were made.

The results were analysed and compared with those of other workers and Niloufer Hospital statistics.

The recovery was assessed by clinical, biochemical and histopathological responses which were studied in four different groups.

Results of therapy with Liv.52 were assessed and compared with control and prednisone treated cases.

A follow-up study was done with special emphasis on hepatosplenomegaly, LFT and repeat liver biopsy.

An attempt was also made to carry out a long-term follow-up study in cases of viral hepatitis particularly to find out the incidence of post-hepatitis cirrhosis.

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