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Acute Infectious Hepatitis with Fulminant Hepatic Failure – A Study of 289 Cases

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Acute infectious hepatitis is by far the most common form of hepatitis. It occurs sporadically and in epidemics. The virus appears in the blood, intestinal contents and liver at various stages of the disease. It is usually transmitted by the faecaloral route. Unsanitary conditions foster its spread especially when human excreta contaminate food or water or where there is more intimate personal contact.

It may have very mild, moderate or severe manifestations. It could be anicteric, but usually, in the majority of cases, jaundice appears. Anorexia, nausea and occasional vomiting which occur especially at the sight of food, are early symptoms. The urine becomes dark brown and a day or two later, frank jaundice appears. Darkening of the urine and a lightening of faeces heralds the development of jaundice starting on the sclera and spreading in varying depths to all over the body. Patients become febrile and feel miserable (Sherlock 1973) [38].

Viral hepatitis, as observed in India, is frequently of prolonged duration with a predisposition to complications like subacute hepatic necrosis or acute fulminant necrosis or acute hepatic failure. Such cases are commonly those in whom a superimposed direct nutritional deficiency increases the susceptibility of the liver cells to necrosis – in Asia and Africa diets usually lack in first class proteins (Davidson 1968)[11]. The development of drowsiness in a patient with acute infectious hepatitis should be regarded as a danger sign. Treatment to prevent complications that are so often the cause of death must be instituted.

Hepatic precoma and coma occur frequently in patients with severe forms of acute viral hepatitis and in severe liver disease. There are several days of confusion followed by stupor, which is a precoma condition and is followed by coma. Hepatic coma is in fact a common accompaniment of most forms of severe liver disease, and hepatocellular failure may follow a severe attack of acute viral hepatitis.

Etiopathological Features

Fulminant hepatic failure is defined as a clinical syndrome associated with massive necrosis of liver cells or with sudden severe impairment of hepatic function. It is characterised by acute onset of progressive and severe mental changes starting with confusion and rapidly advancing to stupor or coma. In nearly all cases there is widespread inflammation in the portal tracts and in the lobules. The cause is presumed to be the virus in most cases (*Brit. med. Bull.* 1972)[6].

The liver undergoes necrosis (Autolysis) and releases breakdown products into the circulation. A great increase of serum amino-acid concentrate is usual when the liver undergoes necrosis. Perhaps these aminoacids are harmful to the brain function when their serum concentration is high. The liver is the chief site for disposal of aminoacids by deamination. Decrease of this function contributes considerably to the hyperaminoacidaemia associated with massive liver necrosis. Coma has been attributed to abnormalities in ammonia metabolism. This, by far, is the most likely hypothesis. The molecular basis of ammonia interaction is not settled though most likely (Sheldon Jacobson 1973)[19]. The cerebral disturbances manifested by patients with liver disease may be the result of many other toxins besides ammonia.

Normally, a great many substances are detoxified and metabolised or excreted by the liver. Some are substances, which depress the cerebral oxygen consumption and brain function, and eventually result in coma.

There is a concept of portal systemic encephalopathy for patients going into coma. The concept considers cerebral intoxication by intestinal contents, which have not been metabolised by the liver, the toxins produced by intestinal bacteria, ammonia toxicity and other nitrogenous substances and L-tryptophane, which is particularly toxic and other metabolic abnormality. These metabolic changes are acid base electrolyte changes, hypoxia, transfer of ionised ammonia across the cell membrane, changes in carbohydrate metabolism, fatty acid metabolism, and undue sensitiveness of the brain to insults. There is difficulty in mobilising and storing carbohydrates and in manufacturing proteins. This syndrome is most frequently associated with viral hepatitis in the fulminant form.

The rapid onset of coma is presumed to be of metabolic origin rather than due to structural changes (Williams 1970)[48]. Disordered cerebral function may be due to a lack of an essential substance produced by the normal liver. Failure of the damaged liver to detoxicate these substances is thought to be the main factor but other metabolic changes as well as alterations in acid base balance and possibly in cerebral blood flow may be additive. Disordered brain function (Encepholopathy) results from substances reaching the brain which are made by bacterial action on protein in the colon due to by-passing the liver cells where they are normally metabolised. The accumulation of toxins especially protein-bound non-dialysable toxins and the lack of essential metabolates may play a part in the pathogenesis of hepatic coma. This, by far, is the most likely hypothesis. The primary site of the action is thought to be on the alerting mechanisms situated in the reticular formation. Recently a lot of interest has been created in the effects of neutrotransmitter amines in hepatic coma. (Parkes *et al,* 1970)[30].

The neurotoxic factor may be responsible for the neurological symptoms. There may be deficiency or absence of one or more substances necessary for cerebral metabolism and synthesised by the normal liver or the presence in excess of one or more substances toxic to the brain which are detoxified or excreted by the normal liver but not destroyed by the liver with fulminant hepatic necrosis. It is not known which of these mechanisms is at work (Geiger and Yamasaki, 1956)[18]. The neurotoxic factor normally destroyed by the liver is ammonia (Benhamou *et al.,* 1961)[2]. Proponents of the neurochemical theory of hepatic coma postulate that there is either a depletion of neurochemical transmitter or norepinephrine and dopamide in certain vital areas of the central nervous system - there are false neurochemical transmitters which displace biologically active neuro-transmitters from neuronal receptor sites (Fischer 1972)[15]. Some studies reveal the potential reversibility of the coma of hepatic failure. One important observation relates to the reversibility of the neurological disorder. However, it is wise to treat all attacks as potentially fatal and to insist upon rest in bed, but allow bathroom facilities.

If deep coma is reached, the prognosis is very poor. It may be that the virulence of the virus in these cases may be greater or the severity of the disease is dependent upon an abnormal reaction of the host. We also do not exactly know the role of immune reactions in the development of this fulminant illness. We also need to know the factors that promote regeneration of the liver and also whether sufficient regeneration of hepatic parenchyma is ever possible after a certain stage of hepatic necrosis has been reached (Sherlock and Parbhoo, 1971)[39] (Willams, 1972)[47].

Clinical Features

Hepatic failure may manifest itself in a number of ways. Hepatic encephalopathy is defined as a neuro-psychiatric syndrome, consisting of intellectual deterioration, altered state of consciousness and abnormal neurologic function in a patient with advanced liver disease (Raskin, 1964)[34]. In the

beginning there may be inappropriate behaviour and agitation followed by progressive lethargy, stupor and coma. Hypoglycaemia, sepsis, electrolyte imbalance, central nervous system trauma and drug intoxication may precipitate precoma or coma. There may be hyperventilation, metabolic encephalopathy, hypoglycaemia and uraemia. In these cases, the immediate problem is widespread and continued loss of liver cells and the resultant encephalopathy is a preterminal event. Drowsiness and coma may be due to failure of the respiratory and vasomotor centres. Unless effective respiration and circulation are maintained further anoxia and cerebral damage are inevitable. Recognition that the illness is progressing toward the severe fulminant stage of massive hepatic necrosis is an indication for immediate intensive care.

The following grades in the development of precoma and coma are described:

Grade I : Minor disorder of consciousness (motor system).
Grade II : Gross disorder of consciousness and disorientation in time and space.
Grade III : Coma.

The stages of the development of hepatic coma can be used as a clinical index of the degree of the liver cell failure present and of the likely prognosis. Changes in mood, confusion or drowsiness are usually the earlier detectable signs. The characteristic-flapping tremor, which is present in the early stages, disappears when the patient sinks into coma. Signs of encephalopathy usually appear with-in a few days of the onset. The whole illness, from the first symptoms to death, may be less than a week. Less frequently the patients have jaundice for a long time–days or weeks–before the appearance of neurological signs.

The clinical picture is a complex one and affects all parts of the brain. The disorder is organic, mental-reaction associated, with a neurological disturbance. Variability is a marked feature. The features differ in activeness and in symptomatology depending on the nature and intensity of etiological and precipitating factors. Children show a particularly acute reaction often with mania. Headache, dizziness, nightmares are inaugural non-specific symptoms, but even before this, the patient may show episodes of antisocial behaviour or character disturbances. Unco-operative behaviour often continues with consciousness clouded. The delirium is of the noisy, restless variety and attacks of screaming occur spontaneously or may be induced by slight stimuli.

Violent behaviour is common in children who may also have fits. Insight into such anomalities of behaviour is frequently present. Speech is slow and slurred the voice monotonous and often faint. In deep stupor dysphasia becomes marked and is always combined with perseveration. Deep tendon reflexes are usually exaggerated although patients during coma become flaccid and lose these reflexes. Plantar response is usually flexor becoming extensor in deep stupor or coma. The clinical course is fluctuant and frequent observation of the patient is necessary. Fetor hepaticus may be detected in the breath. Hyperventilation and hyperpyrexia may be terminal.

Hypersomnia appears early and progresses to inversion of sleep rhythm. Reduction of spontaneous movement, a fixed stare, apathy, slowness and brevity of response are early signs. Further deterioration results in reaction only to intense or noxious stimuli.

Coma at first resembles normal sleep but progresses to complete unresponsiveness. Deterioration may be arrested at any level with either regression or persistence of symptoms. Rapid changes in the level of consciousness are accompanied by delirium.

Personality changes are most conspicuous in association with chronic liver disease. Intermittent changes include childishness, irritability and loss of concern for the family. Intellectual deterioration varies from slight impairment of organic mental function to gross confusion. Daily

fluctuations may be observed. Focal defects appearing in a setting of clear consciousness relate to disturbances in visual spatial gnosis. These are most easily elicited in the motor sphere as constructional apraxia shown by inability to reproduce simple designs–size, shape, structural function – Astereognosis. Changes in the pattern of handwriting are a good check of progress.

The psychiatric syndrome is an acute organic reaction with delirium, disorientation and visual hallucinosis and clouding of consciousness rapidly progressing to coma within hours or days. Mental abnormalities may develop before jaundice or the syndrome may appear when the patient is deeply jaundiced. Tremor may be transient or overlooked, if not carefully looked for.

Serum enzyme levels are markedly elevated and prothrombin time is markedly prolonged. SGOT and SGPT–transaminase levels are more frequently elevated. Serum activity of these enzymes is helpful in detecting the presence or absence of hepatocellular disease in a jaundiced patient. SGOT greatly increases in the serum of patients in the acute phase of viral hepatitis. SGPT also increases in similar circumstances. However, depth of jaundice and height of SGOT and/or SGPT levels are unreliable. They may even fall as the patient's condition worsens.

Cerebrospinal fluid shows normal number of cells and increased protein. Glutamic acid is often increased and also glutamine. Ammonia content is often raised but is poorly correlated with blood. Electroencephalogram may be helpful.

Present Day Status of the Therapy of Fulminant Hepatic Failure

The therapy of acute fulminant hepatocellular failure demands prompt care and attention. Mortality in fulminant hepatic failure is very high, 81% in the first 318 patients who reported to the Fulminant Hepatic Failure Surveillance Study (FHF Surveillance Study, 1969)[17].

Zacharias *et al* (1967)[50] successfully treated 3 cases of hepatic coma due to infective hepatitis out of 11 cases. Sundaravalli and Raju (1973)[42] studied 35 children with hepatic coma due to infectious hepatitis. 10 had exchange transfusions out of which 3 survived and out of the remaining 25 cases 3 survived. Thus in all 6 children survived out of 35 children.

Jones *et al* (1967)[23] had no survivals in 7 cases. Trey and Davidson (1970)[46] had a poor survival rate of only 17.6% in those with stage IV coma, but 66% in those with the stage II encephalopathy.

Saunders *et al* (1970)[37] *Brit. med. Bull.* (Vol. 28, No. 2, 1972)[6] in Cape Town have published results of one of the largest series of cases among their own patients. Their study showed that out of 47 patients 7 recovered consciousness of which only 4 survived. Of 20 patients treated conservatively 4 (20%) survived. This is to be compared to 10 (21%) survivors of the 47 patients treated by exchange transfusion. Some of the initial enthusiasm for this procedure has waned, for, the published long-term results are depressing.

The collected results of the Fulminant Hepatic Failure Surveillance Study (Trey and Davidson, 1970)[46] also need careful scrutiny. Of 101 patients in whom no special procedure was undertaken, 10% survived whilst the survival in 166 patients treated with exchange transfusion was 24%. However, the preliminary results of the first randomly allocated and controlled trial of exchange transfusion in fulminant hepatitis carried out in Los Angeles showed a higher mortality in the treated group (A.G. Redekar and colleagues)[36]. Among 60 patients with fulminant hepatitis there was no significant difference between the survival rate of the patients treated conservatively and the patients treated by corticosteroids and/or exchange transfusion and/or cross circulation and/or hyperbaric oxygen (Benhamou, Rueff and Sicot, 1972)[3].

Exchange transfusion may be used to remove toxic substances from the blood and in particular those that are protein bound and so not dialysable (Trey *et al.*, 1966)[45]. Patients who have been treated with exchange transfusion have a survival rate of approximately 20%.

A recent controlled trial by Redekar and Yamahiro (1973)[35] showed that exchange blood transfusion has failed to maintain its popularity as it showed no benefit. The prognosis is very poor if deep coma is reached, the mortality rate being 90%.

Corticosteroids should not be given routinely. Although they probably have some effect on the healing of the liver, they should be reserved for the patient with prolonged cholestasis or one who seems to be passing into the subacute stage with persistent jaundice and high serum globulin and transaminase values. In chronic cases, which received corticosteroids, it is possible that this treatment may have helped to perpetuate the disease although this has not been proved. It certainly did not prevent the development of chronic sequelae. (Sherlock, 1973,[38] Ducci and Katz, 1952,[13] Bernard *et al,* 1964,[4] Blum *et al*, 1969,[7] Cachin *et al,* 1963 A & B[9,10]).

The outlook of therapy in comatose patients is so poor that a case could be made for corticosteroid therapy. Favourable results have been reported but more usually reported are the failures. Periotoneal dialysis and haemodialysis are certainly useful in the treatment of the uraemic stage. Liver perfusion and hepatic transplantation have also been used experimentally. Hyperbaric oxygen therapy, coenzyme administration, haemodialysis, peritoneal dialysis, exchange transfusion and cross circulation treatment, extracorporeal liver perfusion have been tried.

The aim is to support the failing liver cells till spontaneous regeneration takes place. Major emphasis has to be placed on restitution of hepatic function. Attempts have been made to rectify the metabolic derangements, combat infection and hypoglycaemia, while anticipating restoration of normal liver function by spontaneous regeneration of liver cells. The very rapid onset of coma suggests a metabolic origin rather than structural change and in keeping with this there is equally rapid reversal. Treatment must be adapted to the problem of the individual patient. Results at the same time are depressing and encouraging. Precipitating factors like gastrointestinal haemorrhage or fall in blood pressure, or acute infection in operation should be taken care of.

Bed rest reduces functional demands on the liver. In acute cases it is advisable while the disease is active. In subacute and chronic hepatocellular failure bed rest is continued while improvement is maintained. In static cases after 4 to 5 weeks, the patients may be allowed moderate activity.

Such supportive therapy, which requires intensive medical and nursing care as well as the full range of biochemical and haematological services, is based on the detailed monitoring of almost every organ and system in the body. In the management of these patients, temperature, blood pressure and pulse must be observed 4-hourly. There should be a fluid intake and output chart and if possible daily weighing, daily estimation of haemoglobin and haematocrit level and occult blood in stools. Daily assessment of hepatic size, daily handwriting chart, daily tests of simple arithmetic and ability to copy a five-pointed star with matches. 4-hourly grading, if necessary, of neuropsychiatric status, daily examination of lungs for evidence of infection or oedema and if facilities permit daily serum bilirubin, sodium, potassium, chloride, bicarbonate and urea levels to assess electrolyte equilibrium. All sedatives are contraindicated if the patient is manic or violent. Treatment of precipitant factors like haemorrhage, infection, alcoholism, electrolyte imbalance, minor operations and management of possible harmful effects or over-dosage of morphine or hypnotics is necessary. Bowels should be emptied of nitrogen containing material, by enema or magnesium sulphate purge. Stop nitrogen containing drugs ammonium chloride, urea, stop diuretics and maintain correct caloric, fluid and electrolyte levels. Ensure at least one free bowel movement daily.

The principles in the management are withdrawal of protein, emptying the bowel by enema and neomycin therapy, as these are the standard measures used in the treatment of presumed cerebral intoxication and to reduce bacterial growth in the colon.

At the early stage of anorexia and nausea no benefit accrues from rigid insistence upon a low fat diet. When appetite returns a high protein diet may hasten recovery. In the early stages all dietary protein should be stopped. 1600 calories should be supplied daily as glucose drinks, 20% solution through gastric drip. Alternatively 10% Levulose may be used. Protein has to be completely eliminated from the diet until the protein is alert. In a patient with an episode of coma normal protein intake may soon be restored. In chronic cases protein restriction is needed to control mental symptoms. During recovery, protein is added as 20 g increments on alternate days. The limits of tolerance are usually 40-60 g per day. Exacerbation of symptoms is treated by rest and abstention from proteins. In acute cases, a few days to a few weeks deprivation of protein does not prove harmful and in the chronic group when dietary protein is to be restricted for many months, clinical malnutrition is not seen. In patients with liver disease, nitrogen equilibrium seems to be maintained on severely reduced intake of protein. The risk of temporary restriction is preferable to the hazards of nitrogen toxicity. Vitamins, high carbohydrate diet and dietary supplements are useful.

Scrupulous attention has to be paid to establishing and maintaining the electrolyte and acid base balance. Hypoglycaemia is especially dangerous. The patients have reduced liver glycogen stores and have decreased capacity for hepatic glucogenesis. Hypokalaemia is frequently encountered in patients with fulminant hepatic necrosis (Felig *et al,* 1970)[14].

In case renal failure develops more concentrated solution can be infused with a large vein pump. If symptoms worsen, the regime for the treatment of acute neurological complications should be adopted. Cardio-vascular and respiratory symptoms must receive attention. Surgical exclusion of the colon for the by-passing of colonic toxins, in chronic neuropsychiatric states, needs to be considered.

Neomycin 1 g 4-hourly by mouth may be given for a week. Oral dose of 3-8 g per day or enemata of 1-2 g of Neomycin in 100-200 cc of normal saline may be given.

Neomycin may be beneficial in some patients. However, deafness (ototoxicity) is well documented following the use of neomycin parenterally and orally and after rectal and colonic irrigation. (*The Medical Letter,* Vol. 15, No. 25, December 7, 1973)[25]. Bircher *et al* (1971)[5] found that Lacitulose could be substituted for Neomycin without ill-effects in chronic patients. The dose ranged from 50 to 140 g a day in divided doses.

The use of Levodopa may eventually prove to be an important addition to our therapeutic regimen. Levodopa can be given in an oral dose of 3.5 to 5 g per day in divided doses (Fisher *et al,* 1971 and 1972)[15,16]. Its action is presumably to replete dopamine stores in the central nervous system. Side effects are gastritis and gastrointestinal bleeding. Parenteral use of the drug may overcome the problem.

Measures to lower blood ammonia are helpful. In an attempt to remove toxins that are responsible for hepatic encephalopathy, a number of systemic blood cleansing procedures have to be advocated such as exchange transfusion; peritoneal dialysis, haemodialysis. The last two are especially useful in the treatment of the uraemic stage. Exchange transfusion may be used to remove toxic substances from the blood and in particular those that are protein bound and so not dialysable.

Immunoglobulins prevent clinical viral hepatitis (Pollock and Reid, 1969)[32]. The recent discovery of the monkey as a susceptible animal for transmission of viral hepatitis lends hope that ultimately

preventive inoculation, as for polio, may be developed for fulminant cases. Haemorrhagic diathesis may lead to intravascular coagulation. To prevent microthrombosis of hepatic, renal and intestinal circulation, early and intensive heparin therapy is useful.

The Present Study

There have been no revolutionary advances in the therapy of viral hepatitis and precoma and coma, and the various modes of treatment have little effect in altering the course. The only aim of therapy is to support the failing hepatic parenchyma and help regeneration of liver cells, thus restoring liver function.

Jaffari, (1969)[20] reports that Liv.52 clears jaundice, improves appetite and brings a sense of well-being. He postulates that it has an anti-inflammatory action and advises its use freely since it is free from untoward side effects. Mukerjee (1971),[27] recommended its use in order to prevent a prolonged course of illness and residual cell damage. Mehrotra, (1973),[26] reports that in his series zinc sulphate turbidity, which indicates the serum gamma globulin and hepato-cellular necrosis, also returned to normal. This indicates that the drug helps in the regeneration of hepatic cells damaged during the disease process and prevents further necrosis of the cells. Dayal (1970)[12] reported that jaundice regressed and liver function tests showed improvement. Infiltration of inflammatory cells in the liver tissue was less after Liv.52 therapy and the recovery was quicker.

A large number of workers have reported on the effects of Liv.52, an indigenous compound (The Himalaya Drug Co. Pvt. Ltd.) on the regeneration of the liver cells and its effectiveness in acute infectious hepatitis.

The therapy of viral hepatitis assumes a very significant and important role as death from this disease is much more common in India, due to poorer standards of nutrition, than in the West, though natural clinical cure may occur with or without residual liver cell damage. However, the problem of therapy of viral hepatitis demands an ideal drug with the essential requisites of quicker recovery and convalescence, without residual liver cell damage. The therapy and management of hepatic cellular failure and acute fulminant failure, which occur in severe cases, naturally, is a major clinical and therapeutic problem. Liv.52 has been widely used and reported on for more than a decade and has much published and authenticated data supporting and confirming its beneficial effect in liver damage of varying degrees. Experimental studies on rats and mice by Sheth *et al,* (1960)[41]; Murkibhavi and Sheth (1957)[28]; Karandikar *et al,* (1963)[24]; Joglekar *et al*, (1963)[22]; Patel *et al,* (1963)[31]; Qazi (1965)[33]; Captain and Syed (1966)[8]; Joglekar and Leevy (1970)[21]; confirmed this effect on rats using different methods including the latest method of Indocyanine Green clearance and autoradiographic patterns. Sule *et al,* (1956, 57)[43,44]; by using different parameters have consistently confirmed that Liv.52 accelerates clinical and biochemical recovery. Arora (1969)[1] as also Mukerjee and Dasgupta (1971)[27] observed that in viral hepatitis Liv.52 brought about reduction in the period of illness and residual liver damage and consequent gain in weight.

MATERIAL AND METHODS

This study was carried out at the Kasturba City Fever Hospital (Infectious Diseases Hospital), Bombay, on 289 cases of severe infectious hepatitis associated with precoma or coma. The cases were personally examined, treated and followed up by the author.

The criteria of diagnosis were based on established clinical manifestations and supported by serial laboratory studies and observations. All the cases showed classical manifestations of acute infectious hepatitis and either were in, or went into precoma or coma and associated acute fulminant hepatic failure during the course of the illness and observation at the hospital.

Usually, only severe and serious cases of acute infectious hepatitis seek admission and are admitted at the Kasturba City Fever Hospital and this served as an important basis for study, as over the years there is a background of extensive experience of the clinical course and progress of these cases at this hospital.

Since toxicity studies on animals had revealed that Liv.52 has no acute or chronic toxicity, teratogenic or carcinogenic effect and no effect on fertility and does not cause malfunction of any organ or affect the growth of animals, the drug was freely used in these toxic and fulminant cases.

Liv.52 tablets (The Himalaya Drug Co. Pvt. Ltd.) two t.i.d. were crushed and administered with tube feeding to precomatose and comatose patients. Each tablet of Liv.52 contains:

Capparis spinosa	65 mg.
Cichorium intybus	65 mg.
Solanum nigrum	32 mg.
Cassia occidentalis	16 mg.
Terminalia arjuna	32 mg.
Achillea millefolium	16 mg.
Tamarix gallica	16 mg.
Mandur bhasma	33 mg.

(Prepared in the juices and decoctions of various hepatic stimulants).

The other therapy adopted was standard bed rest, maintenance of fluid and electrolyte balance, glucose–oral and parenteral, restriction of proteins and supplements of vitamins and usual symptomatic treatment. Corticosteroids and neomycin were administered in a few cases with ungratifying results.

Table I: Sex distribution	
Males	126
Females	163
Total	289

There were 126 males and 163 females. The age distribution was as follows:

Table II: Age distribution	
Age in years	No. of patients
1-10	15
11-20	37
21-30	165
31-40	47
41-50	13
51-60	11
61-70	1
Total	289

Maximum age incidence was between the ages of 11 years and 40 years. i.e. a total of 249 cases (86.20% approximately) out of 289 cases. A total of 165 cases (57%) out of 289 were between 21 - 30 years of age.

Fifty patients were admitted in a gasping condition. In spite of treatment 52 died within 48 hours of admission and another 57 died on 3rd and 4th days. Thus 109 patients expired within 96 hours of admission. Liv.52 therapy being oral is expected to take at least 48 hours before clinical effects can be observed. Therefore, in compiling the results, the cases who died within 48 hours of admission, i.e. before the oral drug could act, have been excluded. The duration of stay in hospital in 126

patients who survived was 1 to 10 days in 19 cases, 10-20 days in 63 cases, 21-30 in 28 cases, 31-40 in 12 cases, and 41 to 50 in 4 cases.

Table III: Duration of stay in hospital	
Patients who survived	
Days	No.
1-10	19
11-20	63
21-30	28
31-40	12
41-50	4
Total	126

Table IV: Duration of stay in hospital	
Patients who died	
Days	No.
1	24
2	28
3	26
4	31
5	11
6	15
7	4
8-10	11
11-14	6
Over 14	7
Total	163

Table V: Seasonal incidence			
	L	D	Total
January-March	19	11	30
April-June	24	32	56
July-September	69	89	158
October-December	14	31	45
Total	126	163	289
L = living; D = dead			

The largest numbers of cases were from July to September –158 (i.e. 54.6%) out of 289 cases. Out of 158 patients in this quarter being probably a severe epidemic 89 (56.3%) expired (Table V).

Table VI: Symptoms on admission	
Jaundice	289
High coloured urine	289
Nausea	76
Vomiting	48
Pain in abdomen	82
Fever	41
Semi-consciousness	14
Comatose	47
Oedema	2
Gasping on admission	50

During the course of study blood pressure readings were below normal levels in most of the semicomatose, comatose and toxic patients.

RESULTS OF THERAPY

Laboratory findings showed bile salts and pigments were present in the urine in all the cases. Initially blood bilirubin showed between 21-30 mg% in comatose patients and 15-20mg% in a large number of precomatose patients. In other cases it ranged between 4-15 mg%. In a very few cases was it below 4 mg%. On therapy, 109 patients died within 96 hours of admission. Blood bilirubin was high in most of these cases. Direct blood bilirubin levels were comparatively and proportionately lower in all the cases.

Table VII: Symptoms and signs - 289 cases			
High coloured urine	289 cases	Palpable liver	37
Jaundice	289	Oedema	37
Nausea	105	Responding to painful stimuli	46
Vomiting	114	No response to painful stimuli	44
Pain in abdomen	130	Headache	2
Fever	210	Tachycardia	7
Dull	3	Haemoptysis	1
Drowsy	50	Haematemesis	1

Semi-consciousness	73	Malenae	1
Unconsciousness	117	Bladder distension	2
Giddiness	14	Difficulty in micturition	1
Abnormal behaviour	6	Chest signs	20
Liver tenderness	92		

Routine blood examination showed mild leucocytosis with slight relative polymorpho-nuclear leucocytosis. SGOT and SGPT levels were initially higher and varied from SGOT 93 to 435 units and SGPT from 150 to 675 units and gradually returned to low levels on improvement. Liver biopsy studies could not be carried out as many patients were critically ill and the procedure would be hazardous due to the toxic condition of the patient and the tendency to bleeding. After therapy total blood bilirubin was below 2 mg in a large number of cases that recovered. Blood bilirubin studies were not possible in all cases. Gradual reduction in levels was found in cases, which improved.

Out of a total of 289 cases of acute infectious hepatitis with fulminant hepatic failures, 163 patients (56.4%) expired, 126 were cured and discharged from within 10 days to 50 days (Table VIII).

However, out of the 163 patients who expired, 52 were moribund on admission or expired within the first 48 hours before the oral therapy could act. If these patients are excluded, then from a total of 237 very serious cases admitted at the City Fever Hospital, a large number of whom were in a state of precoma or coma with toxaemia, 126 were cured, giving 53.16% survival rate (Table IX). At no stage did we encounter any sort of toxic or side effects with Liv.52.

Table VII: Results of therapy	
Cured	126
Died	163
Total	289

Table IX: Results of therapy excluding moribund cases	
Total	237
Cured	126
Approximate	53.16%

SUMMARY AND CONCLUSIONS

1. Acute Fulminant Hepatic failure presented clinically as cases of infectious hepatitis with precoma and coma has been studied.

2. Etiopathology clinical features and results of various present-day modes of therapy are reviewed and discussed.

3. 289 cases of acute infectious hepatitis with fulminant hepatic failure are observed and studied for the effects of Liv.52 therapy in addition to the usual conventional modes of therapy at this institution.

4. Age and sex incidence, seasonal incidence and clinical features and results of laboratory findings in these cases are presented.

5. Results show the cure rate of 53% i.e. 126 patients out of 237 patients (excluding 52 moribund patients admitted in a gasping condition and who died within 48 hours of admission before the oral therapy could become therapeutically effective).

6. There were no acute or subacute toxic effects of the drug observed in this study.

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