FULMINANT HEPATIC FAILURE

- A retrospective study in Urumqi, Xinjiang P.R. of China 1999-2004

Jonas Varkey
Antonios Kelepouris

10p Diploma Work in Medicine
Department of Infectious Diseases
Sahlgrenska Academy
Göteborg University

Correspondence
kh00vajo@medstud.gu.se
guskelea@student.gu.se

Supervisors
Zhang Auxin, Professor, First affiliated hospital of Urumqi, Xinjiang P.R.China
Rune Andersson, Professor, Research and Development Centre,
Skaraborg Hospital, Skövde, Sweden
SUMMARY
Fulminant Hepatic Failure was diagnosed in fifty-five patients in Urumqi, Xinjiang, PR China between 1999-2004. Their mean age was 46yrs (6-70yrs). 71% were men. Nineteen patients had an acute FHF. Three patients had an acute co infection with hepatitis A and B, and four patients with hepatitis B and E. One patient had acute hepatitis A with Mb Wilson. For eleven patients the cause of FHF was unknown. Thirty-six patients had a chronic FHF. This was caused by hepatitis B in thirty-three patients (92%). One had hepatitis B and C and two unknown aetiology. The prognosis was poor with mortality on 67%. Treatment was given with Molecular Adsorbent Recycling System (MARS) to eight patients. Only one of them survived and one was lost at follow up. Conclusively, the treatment with MARS has limited value in patients with chronic liver diseases, when curative treatment with liver transplantation is not available.
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INTRODUCTION

Fulminant hepatic failure (FHF) is a severe disease of the liver with lethal complications. The distribution of the disease is world-wide, but the cause varies in between countries. In developing countries the most common cause is viral and in industrialised countries drug induced toxicity predominates. The disease onsets with typical symptoms that indicate liver disease such as jaundice or non-specific symptoms such as fatigue and loss of appetite. The debut of the disease is acute and within a short period of time, patients develop encephalopathy which is the most common complication. Other complications that often lead to death are cerebral oedema and hepatorenal syndrome. It is important to recognise these patients before they develop FHF with complications to decrease mortality. Many patients also have chronic hepatitis which may delay patients from seeking medical care since they think that their symptoms are caused by their chronic disease. Other diseases which may have similar symptoms should be considered as possible differential diagnosis. For example sepsis without liver involvement.

The traditional treatments of FHF are based on stabilisation of vital functions among patients with good prognosis and consider transplantation for those with bad prognosis. During recent years a new method has been developed which not only uses the advantages of normal dialysis but also removes protein bound toxins from the blood. In western countries including Sweden, the dialysis is mainly for patients with toxic FHF and for patients waiting for liver transplantation, whereas in China the aim is to complement the standard treatment. The documentation of this method is still very poor. Another disadvantage is that it is very expensive and not all patients are suitable for it. The traditional treatment is still very useful and combination with this dialysis method might improve the final outcome.

Future treatments involve more pathophysiological methods such as prostaglandins but this is still under trial [10].
2.1 AETIOLOGY

1) Viral
The most common cause world-wide of FHF is viral hepatitis. The cause of FHF varies geographically and is often indeterminate. HBV infections or co-infections with other viruses is the most common cause of fulminant viral hepatitis in developed countries. However, the highest incidence of fatal hepatitis is caused by acute non-A non-B hepatitis [1,2]. Non-hepatitis viruses such as herpes simplex virus, cytomegalovirus, adenovirus, Epstein-Barr virus and varicella have also been shown to cause FHF especially in immunocompromised individuals [3].

2) Drugs/toxins
Hepatotoxic drugs and chemicals are divided into two classes: dose dependent (e.g. acetaminophen, amanita phalloides) and idiosyncratic (e.g. halothane, some NSAIDS, troglitazone). Undefined genetic and environmental factors can cause drug induced hepatotoxicity in any given individual [4].

3) Vascular
Hepatic ischemia caused by Budd-Chiary syndrome, portal vein thrombosis, right ventricular failure or secondary to shock can lead to FHF [4].

4) Metabolic/other
Wilsons disease, autoimmune hepatitis, Reye syndrome, acute fatty liver can also progrediate into FHF [4,5].

2.2 EPIDEMIOLOGY OF HEPATITIS IN XINJIANG
Between 1992-1995 a survey was conducted from the Public Health Institute to investigate epidemiology of hepatitis. The aim of the research was to study the prevalence of hepatitis among different ethnic groups and regions. The study did not however contain information about the clinical presentation of the disease.
The province was divided into 4 regions- North, east, south of Xinjiang and Urumqi. Serum samples were collected from 4610 people in 11 different sampling points across the province. At the north part of Xinjiang 2300 people were tested, in south 1484 people, in the eastern part 427 people were checked and 399 in Urumqi.

Anti-HAV was positive in 89.3% of the patients. No difference was seen between male and female. Highest prevalence was present in ages >10 years old with a peak among 30 years old people. Uygur people living in south region of Xinjiang was the most infected.

Carrier rate of HbsAg was seen in 4.62% with a higher rate among males (117/2210=5.29%) compared to females (96/2400=4%) (p<0.05). Most common age group was ages 5-35 years old. East of Xinjiang had the highest prevalence (37/427=8.67%) and south of Xinjiang had the lowest (28/1484=1.87%). No statistical significant differences were found between men and women or when comparing different ages. There was an indication though that rate of infection increases with age. South of Xinjiang had the lowest prevalence. (256/1484=17.25%). The most common ethic group among the HBsAg-carriers was Han (780/1455=53.61%) followed by Ha (226/878=25.74%) and Uygur (420/1921=21.86%).

Anti-HCV was positive in 3.12%. At the age of 1 year 5.45% was positive with a decrease to 1.97% at the age of 20. Highest infection rate was detected in South of Xinjiang
(63/1484=4.25%) and lowest in east (5/427=1.17%). Different ethnic groups had the same prevalence but Han (42/1176=3.57%) and Uygur (71/1818=3.91%) living in city had higher prevalence compared to Ha (11/724=1.52%).

Anti-HDV was tested among patients who were positive for HBV infection. No case of HDV was however found.

Anti-HEV was positive in 8.63% with no difference between male and female. Those older than 15 years had the highest prevalence (11.45%). No statistic difference was observed between Han (116/1455=7.97%) and Uygur (252/1921=13.12%). Ha however differed from the other groups by having the lowest prevalence (17/878=1.94%) [5].

2.3 DIAGNOSIS
For diagnosing FHF the presence of encephalopathy is required among patients with severe acute liver disease [8]. Diagnosis is difficult because the onset of the disease usually is with non-specific symptoms such as nausea, vomiting, followed by jaundice and rapid development of impaired mental status. The disease can progrediate into multiorgan failure, coma or sepsis. It is important to consider the diagnosis in sick patients in whom an underlying diagnosis is lacking, particularly when coma or metabolic acidosis are present. Differential diagnosis such as drug overdose and Gram negative sepsis needs to be excluded [4, 7, 8].

Clinical picture
• Symptom characteristic for liver disease include jaundice, fatigue and abdominal distension. Clinical findings such as unconsciousness, ascites, leg edema, palmar erythema and spiders occur frequently and are thus an indication of the disease.
• Increased serum ammonium is used to confirm the diagnosis of hepatic encephalopathy and to monitor the success of therapy.
• Liver synthetic function is decreased, which is reflected in an increased prothrombin time (APTT). Increasing or persisting prolongation of APTT is a poor prognostic factor.
• ASAT and ALAT are initially elevated (usually ALAT>ASAT) and decrease as the liver damage progresses resulting in a decreasing liver size.
• Fluid and electrolyte balance disturbances such as hypokalemia, hypofosfatemia (specially in patients with intact urinary outflow) occurs early and can be lifethreating.
• Hypoglycemia may be mild in 50% of cases but can also be profound and complicate the disease.
• Trombocytopenia and multi clotting factor deficiencies (with exception of factor 8) occur as a result of the decreased liver function.
• Increased susceptibility to bacterial infections because of immune suppression is seen.
• ECG findings include multiple VES, heartblocks, bradycardia.
• EEG has characteristic pattern for encephalopathy and could be used for evaluating brain damage.
• Radiology- Ultrasound to investigate the liver size, spleen size, portal vein diameter, splenic vein diameter and measure of ascites volume.
• Serology- To determine the aetiology (HAV, HBV, HCV, HDV, HEV, HGV, CMV, EBV, TTV) of the disease and establish if the disease is acute or chronic. Among chronic patients serology tests are used to exclude co infections [5, 7, 9].
2.4 PATHOGENESIS
Data indicates that irrespective of aetiology of fulminant hepatic failure the result is hypoxic injury and cell death caused by the hosts immune responses [10].

Most hepatitis viruses are non cytopathic. Infected hepatocytes are affected by the host immune responses via major histocompatibility complex because of viral or self antigens expressed on their surface [11]. These immune responses are thereby responsible for both viral clearance and liver injury during infection [12]. Mutations often occur in patients with FHF caused by HBV. These mutations can lead to transcription of the HBV X-protein (HBX) which induces hepatic apoptosis in the early stage of the HBV infection [10]. Hepatocyte functions can be directly affected by viral proteins and become hypersensitive to the cytopathic effect of interferon-gama [12, 13]. Other viral proteins such as nucleocapsid protein (nhv-3) has been postulated induce the expression of FG12-prothrombinase which cleaves prothrombin to thrombin and thereby contributes to the pathogenesis of fulminant hepatitis [10].

Host response
The role of CTL responses
CD8+ CTLs is a important determinant of viral clearance in FHF [10]. Antigen-specific CTL destroy HBV infected hepatocytes and initiate immune response that result in recruitment of other inflammatory cell that can destroy infected hepatocytes [14]. Antigen specific CTL also secrete IFN-gamma which leads to secretion of proinflammatory monokines from the macrophages, this might contribute to the pathogenesis of FHF.

Macrophage activation
Macrophages can produce liver injury by releasing free radicals. Activated macrophages can produce tissue factor and fg12 which disrupt the hepatic microcirculation and result in fibrinoid necrosis [10].

Effects of cytokines
Viral replication triggers cytokine release from the Kuppfer cells. Cytokines (IL-1,IL-6,TNF-a) is essential to the development of liver necrosis [15].

Liver cell apoptosis
Caspases is cysteine proteases which cause hepatocyte apoptosis as a result of host immune response against virus infected cells. TNF alfa also induces apoptosis in hepatocytes. Apoptosis in liver can result in FHF [16].

Coagulation pathway
Coagulation cascade is part of the host inflammation and is activated by bacterial products and viruses. This activation results in the generation of factors which lead to fibrin deposition that causes microvascular thrombosis, leukocyte accumulation and up regulation of the inflammatory response.
2.5 COMPLICATIONS:

Encephalopathy:
A reversible neuropsychiatric syndrome caused by liver disease and usually associated with portal systemic shunting of venous blood [7]. Pathogenesis of encephalopathy is caused by the synergistic effect of toxins acting on nervous system. The toxins consist of substances derived from metabolism of nitrogenous substrate, increased short chain fatty acid in the blood and other compounds. Early recognition of changes in signs and symptoms of encephalopathy is therefore important because it reflects a deteriorating liver function.

The clinical grading of the severity of hepatic encephalopathy is divided into the following:
Grade 1: Poor concentration, slurred speech, slow mentation, disordered sleep rhythm.
Grade 2: Drowsy but easily rousable, aggressive behaviour, lethargic.
Grade 3: Marked confusion, drowsy, sleepy, but responds to pain and voice. Gross disorientation.
Grade 4: Unresponsive to voice may or may not respond to pain unconscious [9].

Cerebral oedema
Is the most common cause of death of patients that have reached grade 4 encephalopathy. Often presents simultaneously with hepatic encephalopathy usually occurring in fast progressing liver failure (<1 week). Traditional signs of increased ICP are hypertension, hyperventilation, bradycardia, increased muscle tone leading to abnormal pupillary reflexes and brainstem respiratory patterns [5].

Renal failure
Often present in patients with a longer duration of illness and may result from acute tubular necrosis (ATN), hepatorenal syndrome (HRS) or volume depletion [4]. HRS is one of the major causes of mortality in patients with fulminant hepatic failure [17].

Coagulopathy
May reflect disseminated intravascular coagulation, vitamin K deficiency or more commonly impaired production of clotting factors. Prothrombin time is a valuable parameter to follow the progress of the patient.

GI bleeding
Acute erosions of stomach and oesophagus are caused by stress.

Metabolic abnormalities
Hypoglycaemia as a result of impaired gluconeogenesis. Hypokalemia and hypophosphatemia often associated with metabolic alkalosis as a result of increased lactate production [7].

Infections
Prevalence approaches 80%. Bacterial infections (staphylococcus, GNR, streptococcus) are most common, occurring specially within the first week of hospitalisation. Fungal infections however tend to occur after the first week among patients with renal failure [4].
2.6 THERAPY:

The aim with treatment of FHF depends on the status of the patient. The key is to maintain the vital functions of the patients with good prognosis until they recover and consider MARS and transplantation for patients with bad prognosis. It is really important to treat the complications of FHF and prevent the pathophysiological mechanisms that often lead to a life-threatening condition.

Stabilization
Provide adequate supportive care to the failing liver, as well as to prevent and treat extrahepatic complications of the disease.

I) Identification and management of complications:

Hepatic encephalopathy
Careful observation and laboratory monitoring are necessary to detect the onset and progression of hepatic encephalopathy. Mild encephalopathy requires restriction of dietary protein, advanced encephalopathy however requires elimination of dietary proteins. Lactulose may help reduce high levels of ammonia and improve the encephalopathy [9].

Metabolic
Hypoglycaemia. Frequent monitoring of blood glucose and continuous glucose infusion.
Hypocalemia-Hyposphatemia

Coagulopathy
May reflect DIC or vitamin K deficiency
Prolonged prothrombin time
Fresh frozen plasma should not be given unless there is active bleeding or an active procedure is planed. A trial of vitamin K may be appropriate.

Renal failure
May result from acute tubular necrosis, hepatorenal syndrome or volume depletion. Distinction between HRS and volume depletion is difficult. May require determination of CVP to assess volume status. Continuous renal support is preferable to intermittent dialysis (continuous venovenous hemodialysis).

Gastrointestinal bleeding
Due to stress. Prophylaxis with H2 antagonists.

Infection
Broad spectrum, non nephrotoxic antibiotics should be considered for deteriorating patients. In case of fungal sepsis fluconazol is recommended. The use of antibiotics is known to be empiric and has not been shown to influence survival.

Cerebral oedema
Immediate goals of therapy are to maintain the intracranial pressure (ICP)<20mmHg and the cerebral pressure (CPP=MAP-ICP)>50mmHg. Measures which appear to be temporarily beneficial in controlling intracerebral hypertension include elevation of the head of the bed to 15-20degrees, mechanical hyperventilation (to a PCO2 of approximately 25 mm hg), intravenous mannitol and barbiturate induced coma [5, 7, 9].
II) MARS

MARS liver support therapy uses the Molecular Adsorbent Recycling System to treat patients with liver failure caused by acute or chronic liver disease. This therapy replaces the detoxifying function of the liver by combining the specific removal of albumin bound toxins with the removal of water soluble toxins in hemodialysis by membrane transport. Molecules larger than 50k Daltons are not removed.

1. The patient's venous blood flow through a catheter via an extracorporeal circuit into the MARS dialyzer and returns to the patient.
2. The outside of this membrane is cleansed by a recirculating human albumin solution. As water and proteinbound toxins are transported, this mechanism produces the driving force for these toxins to pass from the patient's blood to the albumin solution.
3. The proteinbound toxins is then cleansed in three steps in a closed system (hepatic detoxification).
4. First the albumin dialysate is dialyzed itself.
5. The second and third step is the detoxification of the albumin dialysate through an activated carbon adsorber and an anion exchanger (liver detoxification).
6. After this regeneration, the membrane can be cleansed by the purified albumin solution.

Toxins which MARS removes

<table>
<thead>
<tr>
<th>Water soluble</th>
<th>Albumin bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile acids</td>
<td>Ammonia</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Creatinine</td>
</tr>
<tr>
<td>Aromatic aminoacids</td>
<td>Urea</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Urea</td>
</tr>
<tr>
<td>Fatty acids</td>
<td>Copper</td>
</tr>
<tr>
<td>Benzodiazepin like</td>
<td>Iron</td>
</tr>
<tr>
<td>substances</td>
<td></td>
</tr>
</tbody>
</table>
[18]
3.1 Patients and method
The research was conducted at the First affiliated hospital of Urumqi, Xinjiang P.R.China. Data were selected from patients diagnosed with acute liver failure and development of encephalopathy including patients with chronic liver disease with acute exacerbation. Diagnosing the patients was difficult since it was based on different factors such as clinical history, symptoms, signs of liver disease, ultra sound findings, serum samples to determine the pathogenic viral agent and laboratory parameters. A total number of 55 patients were collected from 1999 to 2004. Three of these patients were admitted to the hospital during the seven weeks when the project was conducted.

The information needed was collected with a questionnaire, to determine demographic data, risk factors, aetiology, clinical features and laboratory results. All patients treated with and without MARS were registered at admission and at discharge. For MARS-treated patients we also registered laboratory parameters before and after each treatment. Data was processed based on the number of MARS-treatments and not on the number of patients. Since the study was retrospective, some questions were difficult to answer such as intravenous drug abuse and sexual behaviour. Registration of body weight was made but the significance of this information is questionable since they didn’t register the length. If we had the patient’s length we would have calculated Body Mass Index and checked if this had any effect on the disease and the final outcome.

First affiliated hospital in Xinjiang was funded 1958. The hospital is divided into three departments. The departments are specialised in HIV/ paediatrics, hepatitis and other infectious diseases. About 90% of the patients are admitted for hepatitis or other chronic liver disease related causes. The hospital contains 77 beds and admit 1440 patients annually. The hospital has been awarded by the government as the most advanced hospital in Xinjiang.

3.2 Diagnostic criteria
- Acute FHF- Patients with acute onset of disease and development of hepatic encephalopathy within 8 weeks after start of symptoms.
- Chronic FHF-Sudden progression to acute liver failure and development of complications in a patient with chronic liver disease.

3.3 Statistics
For analyzing our data, approximations of binomial distribution has been calculated. The confidence interval (CI) of 95% was used (Formula: Interval= mean value +/- 1,96*SQRT (p*(100-p)/n), where n is number of observations and p is frequency in %). This was done for those numbers where p*n >500 and (1-p)*n >500 [43].
4 RESULTS

4.1 Demographic data

Our patients are divided into two groups. The first group consists of patients with acute onset of disease and the second group of patients with chronic disease with sudden onset of liver failure. The first group had a mean age of 40 years whereas the latter had a mean age of 49 years. Mean age of MARS treated patients was 46 years. 63% of acute patients were males and 75% of the chronic. Both acute and chronic patients had family members infected (2/19 and 4/36 respectively). There is an over representation of Han nationality in both groups 90% in chronic FHF (32/36) and 68% in acute FHF (13/19).

There is a significant difference in where the different groups live. Most of the chronic patients live in the city whereas most of the acute patients live at the countryside.

The economic status of the patients had no clear relation to the patients education level and work situation. For example, some of the farmers had better economic status than well educated people working at office. 27% of the patients had been operated on and 7% had received blood transfusion.

4.2 Aetiology

HBV was detected in 65 percent of the patients whereas most of them where chronic.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Per cent (95% CI)</th>
<th>Acute</th>
<th>Per cent (95% CI)</th>
<th>Chronic</th>
<th>Per cent (95% CI)</th>
<th>No MARS</th>
<th>Per cent (95% CI)</th>
<th>MARS</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>36/55</td>
<td>65 (52-78)</td>
<td>3/19</td>
<td>16%</td>
<td>33/36</td>
<td>92(83-100)</td>
<td>30/47</td>
<td>64(50-78)</td>
<td>6/8</td>
<td>75%</td>
</tr>
<tr>
<td>HAV</td>
<td>1/55</td>
<td>2%</td>
<td>1/19</td>
<td>5%</td>
<td>0</td>
<td>1/47</td>
<td>2%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBV+HAV</td>
<td>3/55</td>
<td>5%</td>
<td>3/19</td>
<td>16%</td>
<td>0</td>
<td>3/47</td>
<td>6%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBV+HEV</td>
<td>3/55</td>
<td>5%</td>
<td>3/19</td>
<td>16%</td>
<td>0</td>
<td>1/47</td>
<td>2%</td>
<td>2/8</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>HBV+HCV</td>
<td>1/55</td>
<td>2%</td>
<td>0</td>
<td>0%</td>
<td>1/36</td>
<td>1/47</td>
<td>2%</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown cause</td>
<td>11/55</td>
<td>20(9-31)</td>
<td>9/19</td>
<td>47(24-70)</td>
<td>2/36</td>
<td>11/47</td>
<td>23(11-35)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Distribution of different hepatitis virus among the 55 patients. No MARS involves patients that are not treated with MARS. MARS column includes the MARS treated patients.

4.3 Prognosis

<table>
<thead>
<tr>
<th>Prognosis</th>
<th>Total</th>
<th>Per cent (95% CI)</th>
<th>Acute</th>
<th>Per cent (95% CI)</th>
<th>Chronic</th>
<th>Per cent (95% CI)</th>
<th>No MARS</th>
<th>Per cent (95% CI)</th>
<th>MARS</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>37/55</td>
<td>67(54-80)</td>
<td>12/19</td>
<td>63(41-85)</td>
<td>25/36</td>
<td>69(53-84)</td>
<td>31/47</td>
<td>66(52-80)</td>
<td>6/8</td>
<td>75%</td>
</tr>
<tr>
<td>Improved</td>
<td>8/55</td>
<td>15(5-25)</td>
<td>3/19</td>
<td>16%</td>
<td>5/36</td>
<td>14(2-26)</td>
<td>7/47</td>
<td>15(5-25)</td>
<td>1/8</td>
<td>13%</td>
</tr>
<tr>
<td>No change</td>
<td>6/55</td>
<td>11(3-19)</td>
<td>3/19</td>
<td>16%</td>
<td>3/36</td>
<td>8%</td>
<td>6/47</td>
<td>13(3-23)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Gave up treatment</td>
<td>2/55</td>
<td>4%</td>
<td>1/19</td>
<td>5%</td>
<td>1/36</td>
<td>3%</td>
<td>1/47</td>
<td>2%</td>
<td>1/8</td>
<td>13%</td>
</tr>
</tbody>
</table>

Table 2. Final outcome.
4.4 Period of hospitalisation

![Graph showing hospitalisation periods](image)

*Figure 1: Period of hospitalisation.*

4.5 Clinical presentation

1) **Reported symptoms**

Fatigue was the most common symptom among all the patient groups. One of the patients had no record.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Total</th>
<th>Per cent (95% CI)</th>
<th>Acute</th>
<th>Per cent (95% CI)</th>
<th>Chronic</th>
<th>Per cent (95% CI)</th>
<th>No MARS</th>
<th>Per cent (95% CI)</th>
<th>MARS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>44/53</td>
<td>83 (73-93)</td>
<td>11/18</td>
<td>61 (38-84)</td>
<td>33/35</td>
<td>94 (86-102)</td>
<td>38/45</td>
<td>84 (73-95)</td>
<td>6/8</td>
</tr>
<tr>
<td>Abd. distension</td>
<td>36/55</td>
<td>65 (52-78)</td>
<td>9/19</td>
<td>47 (24-70)</td>
<td>27/36</td>
<td>75 (61-89)</td>
<td>31/47</td>
<td>66 (52-80)</td>
<td>5/8</td>
</tr>
<tr>
<td>Nausea</td>
<td>35/53</td>
<td>66 (53-79)</td>
<td>8/18</td>
<td>44 (21-67)</td>
<td>27/35</td>
<td>77 (63-91)</td>
<td>31/45</td>
<td>69 (55-83)</td>
<td>4/8</td>
</tr>
<tr>
<td>Vomiting</td>
<td>16/53</td>
<td>30 (17-43)</td>
<td>6/18</td>
<td>33 (11-55)</td>
<td>10/35</td>
<td>29 (14-44)</td>
<td>15/45</td>
<td>33 (19-47)</td>
<td>1/8</td>
</tr>
<tr>
<td>Fever</td>
<td>6/54</td>
<td>11 (2-20)</td>
<td>1/18</td>
<td>6%</td>
<td>5/36</td>
<td>14 (2-26)</td>
<td>6/46</td>
<td>13 (3-23)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Table 3. The most frequent symptoms among 55 patients with FHF in Urumqi.*
II) Clinical findings
Leg oedema was more frequent in chronic patients. All patients had ascites, whereas unconsciousness was more common among acute patients.

<table>
<thead>
<tr>
<th></th>
<th>Per cent (95% CI)</th>
<th>Acute n=19</th>
<th>Per cent (95% CI)</th>
<th>Chronic n=36</th>
<th>Per cent (95% CI)</th>
<th>No MARS n=47</th>
<th>Per cent (95% CI)</th>
<th>MARS n=8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Icterus</td>
<td>54/54</td>
<td>100%</td>
<td>18/18</td>
<td>100</td>
<td>36/36</td>
<td>100</td>
<td>46/46</td>
<td>100</td>
</tr>
<tr>
<td>Ascites</td>
<td>41/55</td>
<td>75(63-87)</td>
<td>12/19</td>
<td>63(41-85)</td>
<td>29/36</td>
<td>81(68-94)</td>
<td>35/47</td>
<td>74(54-82)</td>
</tr>
<tr>
<td>Leg edema</td>
<td>23/55</td>
<td>42(29-55)</td>
<td>7/19</td>
<td>37(15-59)</td>
<td>16/36</td>
<td>44(27-61)%</td>
<td>18/47</td>
<td>38(22-50)</td>
</tr>
<tr>
<td>Hemmoragia</td>
<td>14/55</td>
<td>25(13-37)</td>
<td>3/19</td>
<td>16%</td>
<td>11/36</td>
<td>31(16-46)</td>
<td>11/47</td>
<td>23(11-35)</td>
</tr>
<tr>
<td>Palmar erytherma</td>
<td>13/55</td>
<td>24(12-35)</td>
<td>3/19</td>
<td>16%</td>
<td>10/36</td>
<td>28(13-43)</td>
<td>11/47</td>
<td>23(11-35)</td>
</tr>
<tr>
<td>Spiders</td>
<td>7/55</td>
<td>13(4-22)</td>
<td>2/19</td>
<td>111%</td>
<td>5/36</td>
<td>14(2-26)</td>
<td>7/47</td>
<td>15(5-25)</td>
</tr>
<tr>
<td>Caput medusa</td>
<td>4/55</td>
<td>7%</td>
<td>0</td>
<td>0%</td>
<td>4/36</td>
<td>11%</td>
<td>4/47</td>
<td>9%</td>
</tr>
<tr>
<td>Liver hypotrophy</td>
<td>20/34</td>
<td>59(42-76)</td>
<td>3/9</td>
<td>33%</td>
<td>17/25</td>
<td>68(49-87)</td>
<td>16/27</td>
<td>59(40-78)</td>
</tr>
<tr>
<td>Portal Vein</td>
<td>8/31</td>
<td>26(10-42)</td>
<td>3/8</td>
<td>38%</td>
<td>5/13</td>
<td>38%</td>
<td>8/27</td>
<td>30(12-48)</td>
</tr>
</tbody>
</table>

Table 4. Clinical findings among 55 patients with FHF in Urumqi.
Reference: portal vein <14mm (male) <12mm (female)
4.6 Complications

Hepatic encephalopathy was the main complication followed by severe bacterial peritonitis in both acute and chronic patients. Among the MARS treated patients unconsciousness was present in 45% (10/22) of the episodes both before and after treatment. An improvement in the grade of encephalopathy was observed in only one patient with Grade 3. No other significant changes were observed.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Per cent</th>
<th>Acute</th>
<th>Per cent</th>
<th>Chronic</th>
<th>Per cent</th>
<th>MARS</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=55</td>
<td>(95%CI)</td>
<td>n=19</td>
<td>(95%CI)</td>
<td>n=36</td>
<td>(95%CI)</td>
<td>n=8</td>
<td></td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>31/55</td>
<td>56(43-69)</td>
<td>9/19</td>
<td>47(24-70)</td>
<td>22/36</td>
<td>61(45-77)</td>
<td>4/8</td>
<td>50%</td>
</tr>
<tr>
<td>Discharge</td>
<td>47/55</td>
<td>85(75-95)</td>
<td>16/19</td>
<td>84(67-100)</td>
<td>31/36</td>
<td>86(74-98)</td>
<td>7/8</td>
<td>88%</td>
</tr>
<tr>
<td>Sp.Bacterial peritonitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>25/55</td>
<td>45(32-58)</td>
<td>3/19</td>
<td>16%</td>
<td>22/36</td>
<td>61(45-77)</td>
<td>4/8</td>
<td>50%</td>
</tr>
<tr>
<td>Discharge</td>
<td>34/55</td>
<td>62(49-75)</td>
<td>12/19</td>
<td>63(41-85)</td>
<td>22/36</td>
<td>61(45-77)</td>
<td>6/8</td>
<td>75%</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>9/55</td>
<td>16(6-26)</td>
<td>1/19</td>
<td>5%</td>
<td>8/36</td>
<td>22(8-36)</td>
<td>1/8</td>
<td>13%</td>
</tr>
<tr>
<td>Discharge</td>
<td>28/55</td>
<td>51(38-64)</td>
<td>11/19</td>
<td>58(35-81)</td>
<td>17/36</td>
<td>47(30-64)</td>
<td>5/8</td>
<td>63%</td>
</tr>
<tr>
<td>Upper GI bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>5/55</td>
<td>9%</td>
<td>0</td>
<td>0%</td>
<td>5/36</td>
<td>14%</td>
<td>1/8</td>
<td>13%</td>
</tr>
<tr>
<td>Discharge</td>
<td>21/55</td>
<td>38(25-51)</td>
<td>7/19</td>
<td>37%</td>
<td>14/36</td>
<td>39(23-55)</td>
<td>2/8</td>
<td>25%</td>
</tr>
<tr>
<td>Pulmonary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>3/55</td>
<td>5%</td>
<td>0</td>
<td>0%</td>
<td>3/36</td>
<td>8%</td>
<td>1/8</td>
<td>13%</td>
</tr>
<tr>
<td>Discharge</td>
<td>6/55</td>
<td>11(3-19)</td>
<td>1/19</td>
<td>5%</td>
<td>5/36</td>
<td>14%</td>
<td>2/8</td>
<td>25%</td>
</tr>
</tbody>
</table>

Table 5. The most frequent complications among 55 patients with FHF in Urumqi.
4.7 Laboratory parameters

I) Liver function test
There were minor changes in the number of pathologic values in bilirubin, ALT and AST when compared admission/ discharge and pretreatment episodes / posttreatment episodes. The median reduction of bilirubin among the MARS treated patients after each treatment episode was 26% but all the patients still had pathologic values. In survivors the median reduction of bilirubin was 38% and in deceased patients 16%.

<table>
<thead>
<tr>
<th>Laboratory Parameters</th>
<th>Admission</th>
<th>Per cent</th>
<th>Pretreatment</th>
<th>MARS</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total bilirubin</strong></td>
<td>49/49</td>
<td>100%</td>
<td>21/21</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32/32</td>
<td>100%</td>
<td>22/22</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td><strong>Direct bilirubin</strong></td>
<td>49/49</td>
<td>100%</td>
<td>21/21</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33/33</td>
<td>100%</td>
<td>22/22</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td><strong>Indirect bilirubin</strong></td>
<td>47/47</td>
<td>100%</td>
<td>21/21</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32/33</td>
<td>97%</td>
<td>22/22</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td><strong>ALT</strong></td>
<td>44/49</td>
<td>90%</td>
<td>20/21</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29/33</td>
<td>88%</td>
<td>20/22</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td><strong>AST</strong></td>
<td>47/48</td>
<td>98%</td>
<td>21/21</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32/33</td>
<td>97%</td>
<td>21/22</td>
<td>95%</td>
<td></td>
</tr>
<tr>
<td><strong>GT</strong></td>
<td>27/47</td>
<td>57%</td>
<td>5/21</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10/32</td>
<td>31%</td>
<td>5/22</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td><strong>Total protein</strong></td>
<td>20/48</td>
<td>4%</td>
<td>7/21</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18/33</td>
<td>55%</td>
<td>9/22</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td><strong>ALP</strong></td>
<td>13/46</td>
<td>28%</td>
<td>3/21</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10/33</td>
<td>30%</td>
<td>2/22</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
<td>44/49</td>
<td>90%</td>
<td>16/21</td>
<td>76%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>29/33</td>
<td>88%</td>
<td>18/22</td>
<td>82%</td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Proportion of patients with pathological liver function tests among 55 patients with FHF in Urumqi. Reference values=total bilirubin: 2~28umol, direct bilirubin: 0~8umol/l, indirect bilirubin: 2-20umol/l, ALT: 0-40U/L, AST: 0-40U/L, GT: 8-50U/L, Total protein: 60-80g/L, ALP: 15-150U/L, Albumin: 35-55g/l.
II) Renal function test
Creatinine was pathologic among 43% of the patients at admission and increased to 81% at discharge. Mean value of creatinine was decreased with 16% after MARS treatment.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Mean</th>
<th>Range (min-max)</th>
<th>Proportion with pathological values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea</td>
<td>Admission</td>
<td>10.9</td>
<td>2.2-30.1</td>
<td>26/46 (57%)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Admission</td>
<td>151</td>
<td>32-360</td>
<td>20/46 (43%)</td>
</tr>
<tr>
<td></td>
<td>Discharge</td>
<td>252</td>
<td>46-1066</td>
<td>34/42 (81%)</td>
</tr>
<tr>
<td>Discharge</td>
<td>17.5</td>
<td>3.6-38</td>
<td></td>
<td>34/42 (81%)</td>
</tr>
</tbody>
</table>

Table 7a

<table>
<thead>
<tr>
<th></th>
<th>MARS</th>
<th>Mean</th>
<th>Range (min-max)</th>
<th>Proportion with pathological values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea</td>
<td>Pretreatment</td>
<td>5.5</td>
<td>1.5-14.4</td>
<td>15/21 (71%)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Pretreatment</td>
<td>85.5</td>
<td>32-296</td>
<td>6/21 (29%)</td>
</tr>
<tr>
<td></td>
<td>Posttreatment</td>
<td>71.6</td>
<td>16-296</td>
<td>4/22 (18%)</td>
</tr>
<tr>
<td></td>
<td>Posttreatment</td>
<td>4.6</td>
<td>1.3-117</td>
<td>13/22 (59%)</td>
</tr>
</tbody>
</table>

Table 7b

Table 7a&7b. Renal function test among 55 patients with FHF in Urumqi. MARS column includes number of episodes of treatment ( not number of patients).

Reference values: BUN: 2.7-7.2mmol/l, Creatinine: 44-133umol/l.

III) Electrolytes
The number of patients with pathologic values of calcium decreased from admission to discharge whereas sodium increased (table 8a). Notice that 90% of the patients had decreased albumin (table 6).

During the MARS treatment we observed an increased number of pathological values for calcium and potassium and an improvement of chloride (table 8b). About 80% had decreased albumin before and after each treatment episode explaining the low calcium level (table 6).

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Mean</th>
<th>Range (min-max)</th>
<th>Proportion with pathological values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca</td>
<td>Admission</td>
<td>2.2</td>
<td>1.3-4.2</td>
<td>18/48 (38%)</td>
</tr>
<tr>
<td></td>
<td>Discharge</td>
<td>2.1</td>
<td>1.0-5.2</td>
<td>12/39 (31%)</td>
</tr>
<tr>
<td>Na</td>
<td>Admission</td>
<td>129</td>
<td>111-146</td>
<td>22/48 (46%)</td>
</tr>
<tr>
<td></td>
<td>Discharge</td>
<td>124</td>
<td>98-147</td>
<td>9/39 (23%)</td>
</tr>
<tr>
<td>Cl</td>
<td>Admission</td>
<td>100</td>
<td>82-114</td>
<td>23/48 (48%)</td>
</tr>
<tr>
<td></td>
<td>Discharge</td>
<td>91</td>
<td>69-111</td>
<td>14/39 (36%)</td>
</tr>
<tr>
<td>K</td>
<td>Admission</td>
<td>4</td>
<td>2.1-6.5</td>
<td>28/48 (58%)</td>
</tr>
<tr>
<td></td>
<td>Discharge</td>
<td>11</td>
<td>2.2-6.8</td>
<td>16/39 (41%)</td>
</tr>
</tbody>
</table>

Table 8a
Ca:
Pretreatment: 2.2
Posttreatment: 2.2

Na:
Pretreatment: 126.4
Posttreatment: 130

Cl:
Pretreatment: 99.5
Posttreatment: 103.3

K:
Pretreatment: 4.5
Posttreatment: 3.9

Table 8b
Table 8a&b. Electrolytes among 55 patients with FHF in Urumqi.
Reference values: Ca: 2.15-2.50 mmol/l, Na: 137-145 mmol/l, Cl: 100-110 mmol/l, K: 3.4-5.4 mmol/l.

IV) Blood glucose
Blood glucose was pathologic in 33% of the patients at admission and 31% at discharge. There were missing data in many patients.

V) Coagulation
98% of all the patients had abnormal PTA at admission (range 8-79%, mean 27.8). New analyses at discharge were only available for a limited number of patients.

Table 9a
Table 9a&b. Coagulation tests among 55 patients with FHF in Urumqi. Reference values: PT: 9-15s, PTA: 70%-110%.
VI) Blood lipids
Blood lipids were checked only at admission for patients not treated with MARS.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Mean</th>
<th>Range</th>
<th>Proportion with pathological values</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG Admission</td>
<td>0.8</td>
<td>0.03-1.8</td>
<td>8/27 (30%)</td>
<td></td>
</tr>
<tr>
<td>HDLD Admission</td>
<td>0.4</td>
<td>0.02-1.6</td>
<td>26/27 (96%)</td>
<td></td>
</tr>
<tr>
<td>CHOLEST Admission</td>
<td>1.8</td>
<td>0.6-5.5</td>
<td>1/27 (4%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 10a

<table>
<thead>
<tr>
<th></th>
<th>MARS</th>
<th>Mean</th>
<th>Range</th>
<th>Proportion with pathological values</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG Pretreatment</td>
<td>0.6</td>
<td>0.03-1.3</td>
<td>3/7 (43%)</td>
<td></td>
</tr>
<tr>
<td>Posttreatment</td>
<td>1.5</td>
<td>0.4-2.8</td>
<td>4/4 (100%)</td>
<td></td>
</tr>
<tr>
<td>HDLD Pretreatment</td>
<td>0.4</td>
<td>0.02-1.2</td>
<td>6/7 (86%)</td>
<td></td>
</tr>
<tr>
<td>Posttreatment</td>
<td>0.2</td>
<td>0.09-0.5</td>
<td>4/4 (100%)</td>
<td></td>
</tr>
<tr>
<td>CHOLEST Pretreatment</td>
<td>1.5</td>
<td>0.35-2.82</td>
<td>1/4 (25%)</td>
<td></td>
</tr>
<tr>
<td>Posttreatment</td>
<td>1.5</td>
<td>0.35-2.82</td>
<td>1/4 (25%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 10b

Table 10a&b. Blood lipid tests among 55 patients with FHF in Urumqi. Reference values: Triglycerider: 0.56-1.7 mmol/l, HDLD: 0.8-2.53 mmol/l, cholesterol: 2.32-5.6 mmol/l.

4.8) Treatment
Most of the patients were treated with vitamin K, H2 antagonists and antibiotics (87%, 73% and 67% respectively).  

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Per cent (95% CI)</th>
<th>Acute</th>
<th>Per cent (95% CI)</th>
<th>Chronic</th>
<th>Per cent (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin K</td>
<td>49/55</td>
<td>89(81-97)</td>
<td>17/19</td>
<td>89(75-100)</td>
<td>32/36</td>
<td>89(79-99)</td>
</tr>
<tr>
<td>+/- Broad spectrum antibiotics</td>
<td>40/55</td>
<td>73(61-85)</td>
<td>12/19</td>
<td>63(41-85)</td>
<td>28/36</td>
<td>78(64-92)</td>
</tr>
<tr>
<td>H2 antagonist/antacids</td>
<td>37/55</td>
<td>67(54-80)</td>
<td>12/19</td>
<td>63(41-85)</td>
<td>25/36</td>
<td>69(54-84)</td>
</tr>
<tr>
<td>Maintain circulating volume with Glucose</td>
<td>33/55</td>
<td>60(45-71)</td>
<td>14/19</td>
<td>74(54-94)</td>
<td>19/36</td>
<td>53(36-70)</td>
</tr>
<tr>
<td>fresh frozen plasma</td>
<td>40/55</td>
<td>73(61-85)</td>
<td>12/19</td>
<td>63(41-85)</td>
<td>18/36</td>
<td>50(33-67)</td>
</tr>
<tr>
<td>Lactulose</td>
<td>20/55</td>
<td>36(23-49)</td>
<td>4/19</td>
<td>21%</td>
<td>16/36</td>
<td>44(27-61)</td>
</tr>
<tr>
<td>N-acetylcysteine</td>
<td>9/55</td>
<td>16(6-26)</td>
<td>2/19</td>
<td>11%</td>
<td>7/36</td>
<td>19(6-32)</td>
</tr>
<tr>
<td>Antifungals</td>
<td>5/55</td>
<td>9%</td>
<td>1/19</td>
<td>5%</td>
<td>4/36</td>
<td>11%</td>
</tr>
</tbody>
</table>

Table 15. Treatments among 55 patients with FHF.
5 Discussion

5.1 Demographic data
There is a possibility that the under representation of the female gender is due to a less frequent risk behavior concerning drug abuse and multiple sex partners. Relatively few studies have been done in the epidemiologic field regarding demographic data. The only article found was in Japanese and we had difficulties in translating the information.

5.2 Possible aggravated factors
Some of the possible risk factors that were of significance to be studied were intravenous drug use and sexual behavior. Since intravenous drug use and sexual intercourse are a common way of transmission in HCV and HBV, it would have been valuable information in the patients’ case histories. Unfortunately, this kind of information was not available since there was no record about it. Our Chinese supervisor explained to us that sexual behavior was a private matter and that the patient would never admit to his physician about abuse of illegal substances. Operations can have been a possible way of transmission. 27% of the patients had been operated on. Most of the operations involved the gastrointestinal tract. The significance of blood transfusion is not clear since only 7% of the patients received blood.

5.3 Aetiology
HBV was the most common cause as it was present in 43 of 55 patients (78%) whereas 9 of 19 (47%) patients were acute. This correlates with other studies done in Asia where 74% of the patients had FHF caused by HBV [19]. This phenomenon is also observed in developed countries [10]. Co-infections with HBV were frequent and observed in 6 of 19 patients (32%) with acute liver failure which confirms other studies that have shown HBV to play an important role in acute fulminant hepatic failure as aetiologic agent or as an aggravating factor [20].

HAV infection alone and not as a co-infection with other viruses was rare and found in only one patient. In our study as in one performed in Senegal and Tunisia, HAV was uncommon cause of FHF [21]. This is probably due to an asymptomatic HAV infection occurred during early childhood [22]. Our HAV infected patient was only six years old with Wilson’s disease (WD) and that confirms the fact that HAV can occasionally cause FHF during early childhood especially among patients with preexisting liver disease. WD which was probably aggravated by HAV lead to FHF. Wilson’s disease (WD) is an autosomal recessive disorder of copper metabolism. Excretion of copper is impaired leading to excess copper that induces free-radical reactions and lipid peroxidation. This results in liver damage that is occasionally followed by FHF [23]. We don’t know if HAV complicated WD and lead to development of FHF but we assume that this was the case since WD alone and HAV alone is rare causes of FHF [24].

Acute hepatitis A was the cause of FHF in 3 patients with chronic hepatitis B. These results agree with the findings from other series [26]. Acute hepatitis E was the cause of FHF in 3 patients with chronic hepatitis B. Similar results have been shown in other studies where 74% of HEV infected patients had evidence of acute or chronic HBV. This indicates that HEV is not alone the cause of FHF in non-endemic regions [20]. Patients with HEV as the cause of FHF in an endemic region have been described in the area of Ili 1995. Ili is located about 500 kilometers from Urumqi and might have influenced the prevalence of HEV in Urumqi [6]. HCV and chronic HBV were seen as a co-infection in only one patient. A study in Asia showed that HCV RNA positivity was 43-59% in patients with FHF of indeterminate cause [27]. However none of our patients with indeterminate cause was positive for HCV RNA. No serological markers were found in 11 of 55 patients (20%). 9 of these patients were acute.
The diagnosis of these patients was therefore classified as “indeterminate” etiology. Similar results are published in several studies. For example in a study made in USA and India, 18% and 15% respectively of the patients had an indeterminate cause of FHF [29,30].

5.4 Reported symptoms and clinical findings
As expected most patients had symptoms compatible with severe liver disease. Among the first symptoms presented, fatigue and nausea were the most common, especially in acute patients (89% and 68% respectively). Chronic patients may have tolerated fatigue better because their habitual status includes this symptom. All patients developed jaundice sooner or later and this agrees with the literature where jaundice is described as the most common symptom [9]. Abdominal distension was mainly in chronic patients (75%) and half of the acute patients. It is possible that portal hypertension (that probably caused abdominal distension) was more profound among chronic patients. Only 11% of patients had fever probably because of infections.

5.5 Management
As already mentioned under “therapy” the major goal in management is to support the failing liver as well as to prevent and treat extra hepatic complications. Supportive care by vitamin K was provided to most of the patients (17/19 of acute and 32/36 of chronic patients). Lactulose was used by 21% of acute and 44% of chronic patients and did not seem to influence the prevalence of hepatic encephalopathy. This disagrees with the result of another study but our patients were treated during a short period of time which may have influenced the results [31].

N-acetylcysteine was administered in only 16% of the total number of patients although many studies suggest that its administration should be considered in all patients with liver failure [32]. According to a study N-acetylcysteine improves serum coagulation factors and prevents progression of encephalopathy. Unfortunately none of these beneficial effects could be proved in our study, because this information was not included in our data collection.

Antibiotics were given to 73% of patients. This was not surprising since using antibiotics as a prophylaxis is a routine.

As presented in other articles the blood volume is usually maintained with colloid [8]. For our patients this glucose was used instead, often in combination with fresh frozen plasma (FFP). According to an article FFP should not be given unless there is an active bleeding [4]. In our study 40 of 55 patients were treated with FFP although only 14/55 had an active bleeding. We didn’t study the significance of this treatment strategy and cannot therefore evaluate it. We don’t know if the difference in treatment is important. A significant number of patients were not tested for many laboratory parameters at discharge. This makes it difficult to compare parameters from admission to discharge and thereby evaluate the importance of the results.

Chinese medicine (CM) is used in many fields of medicine but when it comes to treatment of liver failure, it’s known that it is more often the cause of the disease rather than the treatment for it. Many CM are hepatotoxic herbs and patients treated with them have worse prognosis, according to an article [33]. Since many of our patients were diagnosed with chronic hepatitis it is likely that many of these patients were treated with CM that might have been hepatotoxic and thereby contributed to their liver failure. Unfortunately, there was no record if our patients were treated with herbs before admission to hospital. Enhanced awareness of herbs’ hepatotoxicity is therefore required especially among patients with liver diseases.
5.6 MARS-treatment
Eight patients with liver failure caused by chronic HBV with exacerbation (75%) and chronic HBV with acute infection (25%) were treated with MARS. Data from laboratory tests were collected before and after each treatment.

The median reduction of bilirubin after the treatment period was 26%, which agrees with the results of another study (-28.3%) [34]. All patients had pathologic bilirubin before and after treatment though. A decrease in blood urea nitrogen levels (from mean 5.5 to 4.6) and encephalopathy grade was also observed which correlates to a study [35]. However, the decrease in encephalopathy was only observed in one patient. Water-soluble substances like creatinine decreased with 14% (mean value). The creatinine correlates well with another study [36]. Effects on ALAT, ASAT is like bilirubin hard to evaluate since almost all the patients had pathologic values before and after treatment. ALP decreased from 14% pathologic results to 9% pathologic results. We observed improvement of chloride after MARS treatment. This contradicts a study where electrolytes weren’t changed after treatment [36]. 80% had decreased albumin before and after each treatment episode explaining the low calcium level. Even if our laboratory parameters correlates well with other studies, the outcome of the patients is very poor (mentioned below). The cause of this is probably multifactoriel. One cause is that the selection of the patients has affected the possibility of recovery as our patients were terminal ill in their chronic liver disease. The follow up between MARS treatments were not standardised. Our study contradicts another study where all patients demonstrated improvement in encephalopathy and 63% survived [37]. The laboratory parameters we have studied are based on each treatment episode and not on each patient. This differs from the articles we have compared our results with since they register each patient. Despite the poor outcome of MARS in our study we believe that it is a promising method and should be applied among patients with acute FHF or as a bridge to transplantation. Our study concluded and confirmed that MARS has positive effect on many lab parameters. It also concluded that it has questionable results when patients have one treatment as well as several treatments without proper follow up.

All patients treated with MARS had good economy and could afford at least one treatment. None of them could afford liver transplantation. Some patients that stayed in hospital during a long period of time acquired financial problems and thereby suddenly stopped treatment. Other patients were forced to leave the hospital in order to save money for their families.

Other reasons such as religion also influenced prognosis. Muslims for example had the desire to die at home, which resulted in that some of them with fatal prognosis left the hospital without completing their treatment. Conclusively, prognosis and economic status were strongly related to each other and should be considered when evaluating our results. Unfortunately, that was difficult; we therefore recorded medical status of our patients without considering their economic situation.

Our conclusion is that the indication for MARS treatment in Urumqi should be used for acute patients with probable reversible failure since transplantation isn’t possible.
5.7 Outcome
The survival among the patients was poor with mortality on 67%. For the patients with acute FHF the mortality was 63% compared to 69% in the group with chronic FHF. 16% and 14% improved during their hospitalization. The mean age of acute patients was 40 years and chronic 49. There was no change in bilirubin, creatinine, prothrombin between acute and chronic patients at discharge. All patients developed hepatic encephalopathy either at admission or during their hospitalisation. Totally about 85% had hepatic encephalopathy and 62% had spontaneous bacterial peritonitis when discharged (other infections were present as well). Hepatorenal syndrome was observed in 58% of acute and 47% of the chronic patients. According to other studies, age >40yrs, serum bilirubin > or = 15 mg/l, prolongation of prothrombin time with >25 seconds, serum creatinine >110mmol/l are poor prognostic factors [38, 39]. Only one or two of these parameters are needed for a poor prognosis. Our patients were positive for atleast one of these factors and that explains the high mortality rate in our results. These numbers confirm that the given factors are poor indicators.

Prognosis did not differ for patients treated with MARS. Surprisingly only one MARS treated patient improved whether 75% (6/8) patients died. The mean age of MARS patients was 46 years. Serum bilirubin was pathologic for all patients. 95% had prolonged prothrombin time and 18% had pathologic values of serum creatinine after treatment. SBP was present in 75% (6/8) of these patients. All patients developed HE and a significant number of them had HRS. According to a research studying the effects of artificial liver support system, the survival rate was 55%. This contradicts our study [41]. The poor prognostic results shown among MARS treated patients compared to the reviewed articles could be because of the selection of patients, low number of patients and economic factors. Previous studies of MARS have been done on acute liver failure with the intention to cure the patient or as a bridge to liver transplantation. Our patients were not collected with the same intention because most of them had an exacerbation of their chronic liver disease. Prolonging their lives was the realistic aim for these patients. A successful treatment for them could therefore be liver transplantation after MARS treatment. Otherwise it is only 20% of patients that spontaneously recover after standard therapy [42]. The higher mortality seen in our patients can’t be correlated since the patient group is different.
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6 References


