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ORIGINAL ARTICLE

Triggers for de-compensation of Chronic Liver Disease in South of Lahore

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ABSTRACT

Background: Cirrhosis is a leading cause of mortality and morbidity across the world with cases number estimated to be as high as 1.5 Billion. Pakistan is one of the countries where the burden of disease is significantly high.
Aim: To understand potential causative factors contributing towards decompensation of liver disease and report it for the benefit of other units providing service to similar population.
Study design: Prospective observational study
Methods: Common complications of portal hypertension resulting from chronic liver disease include development of ascites, encephalopathy, GI bleeding and hepato-renal syndrome. Decompensation of cirrhosis can be transient with full recovery (re-compensation), or it can be chronic. During an event of acute decompensation, clinicians strive to treat the underlying trigger which may have resulted in decompensation alongside the supportive treatment. Several of such potential factors have been reported in the literature. New infection, dehydration, consumption of alcohol and new medications are a few to mention. Many a times the cause of decompensation remains unclear.
Results: The patients with established cirrhosis can develop such complications of the disease resulting in what is known as decompensation at any point during disease. It is imperative for a liver unit to know the relevant causes of hepatic decompensation in its own patients so that the treatment is based on the evidence from local population; the data which is scarce.
Conclusion: Non-compliance with medical advice was the commonest factor as opposed to the available data most of which reports infection as the commonest factor, although infection was the second most common factor, and the commonest concomitant factor in this subset of patients. Cause of decompensation remains unidentified in over one fourth of cases.
Keywords: Decompensation, trigger, chronic liver disease

INTRODUCTION

Cirrhosis is the 11th leading cause of death globally accounting for approximately 2 million deaths per year worldwide[1]. Burden of disease and underlying causes differ across locations and demographic groups[2]. Asia Pacific region shares more than half of the global deaths annually due to Cirrhosis[3]. Burden of disease is very significant in Pakistan and viral hepatitis (B & C) is the commonest underlying aetiology accounting for over 70% of Cirrhosis related deaths[3]. Decompensated cirrhosis defined as an acute deterioration in liver function in a patient with cirrhosis is characterised by jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome or variceal haemorrhage[4]. It is a frequent reason for acute hospital admissions and has significant in-hospital mortality of 10-20% in countries with excellent health system e.g. UK[4] Common precipitants of hepatic decompensation include infections, gastrointestinal (GI) bleeding, high alcohol intake / alcohol-related hepatitis or drug-induced liver injury although no specific cause is found in approximately 50% of cases[5]. Other reported potential contributors include constipation, dehydration, ischemia, hepatocellular carcinoma and portal vein thrombosis[6]. An important observation of clinical practice at our unit is that such published data may only partially be relevant to our population and other factors e.g. poor compliance with prescribed medication and advice including follow up may also be identified as contributing towards hepatic decompensation. It is important to determine the underlying cause of decompensation of Cirrhosis through a careful history, examination and investigations so that appropriate treatment can be given, as this can be life-saving[4,7].

Therefore we planned this prospective study to identify the potential precipitating factors which are more relevant to our practice and perhaps in the wider population around us in 2nd largest city of the country.

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MATERIALS AND METHODS

This was a prospective study. After approval from the ethics committee, data was collected from the clinical notes of all adult patients (defined as those above 18 years of age) admitted to our unit with the diagnosis of decompensated chronic liver disease during the calendar year 2021. Patients with non-cirrhotic portal hypertension were excluded from the study. Consent to participate in the study was obtained from the patients at the time of consent for the treatment before admission to the hospital. The following data was populated on a Microsoft Excel spread sheet. Hospital number, Age, Gender, Underlying aetiology of cirrhosis, whether this was the index presentation, Features of decompensation, Identified contributor and the outcome. Hospital number was used as the unique identifier of the patient. A subsequent presentation of the same patient during the study period was given an additional number to include as a separate hospital admission, as there could have been two different reasons for decompensation on two different occasions. Age and Gender were used as the epidemiological data and were documented as advised by the patient. Underlying aetiology of the patient was either identified for the first time if this was an index presentation or taken as it was documented previously if work-up had been completed in the past. Co-factors to cause Cirrhosis were present in many and all co-factors were added to the data. We divided the underlying aetiology of cirrhosis into four broad categories i.e. Chronic viral hepatitis (mainly B & C), NASH, Alcohol, and “Others” which would include causes of Cirrhosis including Autoimmune liver diseases, Biliary diseases e.g. Primary sclerosing cholangitis, primary biliary cholangitis and secondary biliary cirrhosis, Storage disease e.g. Haemochromatosis, Wilson’s disease, alpha-1 antitrypsin deficiency and other rare disease such as Budd-Chiari syndrome, CF related liver disease, cardiac or cryptogenic cirrhosis and tropical liver disease.

We also documented if this was the index presentation i.e. first presentation with a complication of cirrhotic portal

hypertension or if the patient had had decompensated in the past. Among the features of decompensation we included the followings in our data. Jaundice, Ascites, Hepatic Encephalopathy, Hepatorenal Syndrome and variceal haemorrhage

Jaundice was defined as bilirubin level elevated above the normal lab range. Ascites was included only if confirmed with ultrasound to ensure patients with clinically un-detectable (minimal & mild) ascites are included and central (abdominal) obesity is not misdiagnosed as presence of ascites. Diagnosis of hepatic encephalopathy was established clinically as described and graded by Westhaven criteria. Any grade of severity of encephalopathy was accepted as "present" for the data analysis. Ammonia levels are not performed routinely at our unit as the most recent data suggests that Ammonia level has little clinical significance in the context of encephalopathy in chronic liver disease (as opposed to acute liver failure where it has particular prognostic value). Diagnosis of variceal haemorrhage was based on clinical history and endoscopic findings. Diagnosis of hepato-renal syndrome was based on criteria described by International Ascites Club[8].

For the potential precipitating factors, we looked for the following. Infections, gastrointestinal (GI) bleeding- variceal or non variceal, high alcohol intake / alcohol-related hepatitis, drug-induced liver injury, constipation, dehydration, ischaemia, hepatocellular carcinoma, portal vein thrombosis and non-compliance with prescribed medication.

Diagnosis of infection was based on clinical presentation and investigations. Admitting clinician's discretion played an important role in this and was accepted if any of the following was present. Fever, clinical evidence of an infection (e.g. cellulitis), Laboratory evidence for example raised white cell count, CRP or ESR than baseline (if available and in the absence of any non-infective inflammatory condition), evidence of SBP on diagnostic ascetic tap (WCC more than 500 and Neutrophil count more than 250/mm^3), positive urinalysis for urinary tract infection, positive culture (blood, urine or from any other sample) and radiological evidence of an infection (e.g. pneumonia). Infection of any site and any kind (including acute viral hepatitis) was accepted as present for the data. We did not expand on the site and type of infection in our data for simplification of this particular study.

Gastro-intestinal bleeding was included as documented by the clinicians in the clinical notes based on the clinical history of haematemasis (or coffee ground vomiting) and melaena and supporting evidence from the labs (e.g. reduction in haemoglobin level with rise in urea level disproportionate to creatinine) as well as findings during endoscopic examination. Both variceal and non-variceal bleeding was included as a single entity for potential contributor towards hepatic decompensation.

Alcohol intake, if any, was documented based on history from patients (or the relatives). Serum ethanol levels were not performed. Drugs were accepted as contributor if a new drug (or higher dose) was taken within last 4 week. Constipation was defined as no (or reduced than usual) bowel movement within last 24 hours. Dehydration was included if this was documented in the examination findings at the time of presentation. Ischaemia was included if this was suspected by the treating doctor as a diagnosis in the correct clinical context e.g. with evidence of ischaemic hepatitis. HCC was included if this was confirmed by a triple phase CT scan, dynamic MR scan or by histology to avoid inclusion of non-HCC lesions. Finding of the portal vein thrombosis (partial or complete) on Doppler ultrasound scan was accepted as sufficient evidence to include in our study although in clinical settings almost all such patients would go on to have a triple phase CT Scan. A new lesion over 1cm was considered as new event in those with previously diagnosed HCC. The inclusion of non-compliance with prescribed medicine and/or follow up was based on the history from patient and collateral history from reliable source (patient and/or relatives)

RESULTS

One hundred and forty seven hospital admission episodes were recorded during the study period. No cause of decompensation could be found in about 28% cases (n=46). 106 admissions episodes therefore were included in the study for 90 patients in whom the decompensation could be attributed to some cause. 5 patients were admitted twice. One patient was admitted 5 times and two patients were admitted thrice. Out of 90 patients, 37 were females (41.1%) and 53 were males (58.9%).

Chronic Hepatitis C was the leading aetiology of cirrhosis, being present in 81.1% of hospital admissions (n=86). 15 hospital admissions (14.1%) had chronic hepatitis B as the underlying aetiology of cirrhosis. No patients were co-infected. 4 hospital admissions were for 1 patient who had NASH and 1 patient who Alcohol had related liver disease was admitted twice. No patient with rare causes of liver disease was admitted with decompensation. Among those with chronic viral hepatitis B or C, other risk factors for liver disease were also present potentially contributing to the development of cirrhosis. Obesity and/or diabetes were present in 22(20.7%) of patients as a co-factor to chronic viral hepatitis. 3% of those with chronic viral hepatitis admitted to drinking alcohol in excess. Fifteen hospital admissions out of 106 were for the 1st presentation of chronic liver disease, presenting in decompensated state (Index presentation). 6 of these patients had a second presentation during the study period. It maybe that those presenting later during the study period would also re-present soon after the 1st episode and the data is not collected.

Symptoms and signs of manifestation of decompensated cirrhosis: Among the symptoms and signs of manifestation of decompensated cirrhosis, following findings were noted as shown in table 1.

Table 1

Symptom or Sign of decompensated Cirrhosis	Percentage Presence in study population
Jaundice	47%
Ascites	73.5%
Encephalopathy	43.1%
Upper GI Bleeding	35.8%
Hepato-renal syndrome	20.7%

Raised bilirubin although present in nearly half (47%) of the cases, in itself it was never an isolated presentation and was accompanied by at least one more symptom or sign.

Ascites was the commonest presentation being present in 78 of the hospital admissions (73.5%). Re-admission rate was the highest among this group, which may be false positive. The reason for this is because centre at present does not have a facility for day case large volume paracentesis and all patients with refractory ascites on long term paracentesis pathway have to be formally admitted and such admissions are not necessarily due to a new event of decompensation. Ascites alone was present 27 times (25.4%) and was accompanied by other factors in remaining 51 patients. Peripheral oedema as part of fluid retention was present in 30 out of 78 patients with ascites.

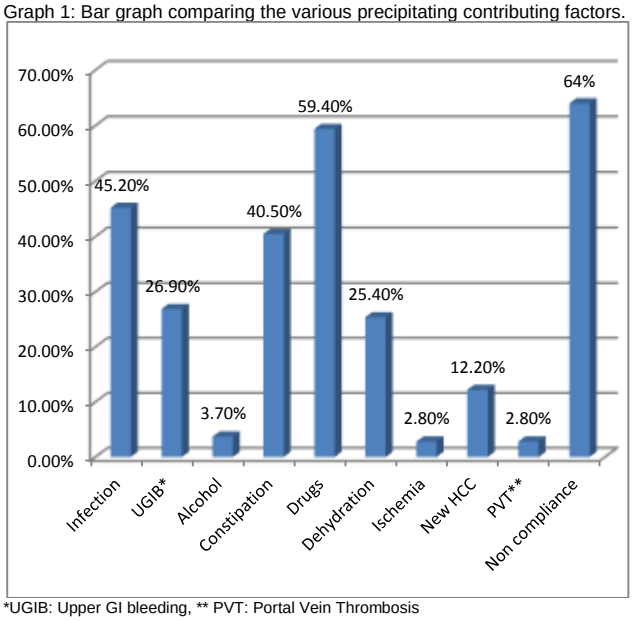
50(47.1%) patients had hepatic encephalopathy. Only a small proportion of these patients (3 patients) had encephalopathy as sole presentation. Among the other manifestations in this group, ascites (29 patients) and variceal bleeding (16 patients) were the commonest.

38(35.8%) patients had variceal GI bleeding. 26 patients had GI bleeding as the only or primary indication for admission. In remaining, ascites was the commonest (16 patients) associated manifestation of decompensation. Hepatic encephalopathy was present in 14 patients (alongside ascites in 4). Variceal bleeding was identified during hospital admission in 12 patients. It will be hard to conclude if this information was missing at the time of history taking or the patients actually bled during hospitalisation indicated by a different reason.

Acute kidney injury as defined by RIFLE criteria was identified at admission bloods in 41 patients. 34 of these patients had ascites present and 10 had GI bleeding. Among those 22 patients fulfilled criteria for HRS. Ascites was obviously present among all of these 22 patients.

Precipitants contributing to decompensation: A single precipitating factor was present only 9 times. There was at least one more contributing factor in the remaining. More than 2 precipitating factors were identified in 27 cases.

Graph 1: Bar graph comparing the various precipitating contributing factors.



*UGIB: Upper GI bleeding, ** PVT: Portal Vein Thrombosis

Infection, as defined by the evidences taken into account described above, was suspected in 48 patients (45.2%). Definite source of infection was found in 20 cases. Decompensation event was presumed to have been caused by GI bleeding in 28 (26.9%) episodes of hospitalisation (26 variceal, 2 non-variceal based on subsequent endoscopic findings). Recent alcohol consumption caused decompensation in 4 patients. Constipation was reported 43 times (40.5% of hospital admissions). New drugs of some kind were reported in 63 cases (59.4%). An observation was made that most of the time the history of new drugs was present but remained unidentifiable and often prescribed by non-specialists or unqualified personnel. Some evidence of dehydration was documented 27 times (25.4%). A plausible explanation for this finding was provided by the observation that almost all such patients were admitted during the summer months. Ischaemia was found to be responsible in 3 cases. All three of these cases had undergone major surgery under general anaesthetic. HCC (or a new lesion) was diagnosed during the event of decompensation in 13 cases. A new portal vein thrombosis was identified in 3 cases. Non-compliance with medication or medical advice provided by hepatology service to prevent complication of cirrhosis was reported in 68 cases (64%).

DISCUSSION

This was a single centre, prospective study with a sizeable number of patients. The study was performed with a view to answer an important clinical question raised from an observation during our day to day clinical practice. The results are interesting and may act as a stimulus to perform a large multi-centre prospective study with an aim to add some evidence for development of national guidelines based on our own data.

Decompensated liver disease carries 85% five year mortality rate without liver transplant and complications. It is an undisputed fact that treating the precipitating cause(s) of decompensation of liver disease is likely to improve the patient outcome. However, in about half of patients, the cause remains undetermined and the treating clinicians have no choice but to treat empirically. Empirical/ initial treatment must be based on the knowledge of data from the population served by particular firm and therefore performing such a study is important.

The study provided valuable information to validate the available data as well as additional relevant information to confirm our hypothesis. We aim to address the issue of non-compliance in our patients through a structured programme and a follow up paper will be submitted for publication as soon as it is completed.

CONCLUSION

Viral hepatitis (B & C) was the leading cause of cirrhosis. Fluid retention i.e. Ascites & oedema remained on top of the list amongst the manifestations of decompensated cirrhosis followed by GI bleeding in our patients. Non-compliance with medical advice was the commonest factor as opposed to the available data most of which reports infection as the commonest factor, although infection was the second most common factor, and the commonest concomitant factor in this subset of patients. Cause of decompensation remains unidentified in over one fourth of cases.

Conflict of interest: Nil

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