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# VARIOUS SCORES USED FOR PROGRESSION OF LIVER DISEASE

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**ABSTRACT:** Multiple causes of liver diseases that will affect the health related quality of life and are dispersed globally. It is difficult to diagnose the different stages of liver disease. Scores like Child Pugh Score(CPS), Model For End Stage Liver Disease(MELD), Monoethylglycinexylidine(MEGX), Von willibrand factor (vWF) etc are used to detect the progression of liver disease like hepatitis, cirrhosis, fibrosis etc. Child Pugh Score is important and traditional component for evaluation of liver disease. It is easy to perform at bed site. MELD is for predicting short term mortality and is more objective but not superior to CPS due to some reasons. These scores contain subjective as well as objective parameters for better prediction of liver related disease. MEGX and von villibrand factor are better simplest markers for the prognosis of liver disease. MEGX is competent to various scores and useful marker for impaired metabolic activity and blood flow in cirrhotic patient. vWF is new non invasive method for survival rate of patient with compensated and decompensated liver disease. By using these scores, we will early detect the disease and preventive measures are taken to improve it. Hence the quality of life is improved if proper medications are taken to improve the health of liver.

**INTRODUCTION:** There are multiple causes of liver disease and it is difficult to diagnose them. Fatigue, nausea, jaundice, pain over the right upper part, fever and various other symptoms that not explained properly so they need medical advice. The different clinical and biochemical parameters are done to predict more accurately the prognosis of patient and assess their survival rate. The major cause of death in the united state is considered to be the End stage liver disease and its treatment is the major problem in public health. Although there are 100 forms of liver disease caused by various factors and it affect everyone from infant to older adults. The diseases are cirrhosis, fibrosis, viral hepatitis. The conventional liver function tests assess only the presence or absence of hepatocellular injury but the quantitative assessment are not determined.

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Different scores are used to diagnose the liver disease or the stage of disease like Child-Pugh score, Model for end stage liver disease (MELD), Monoethylglycinexylidine (MEGX) and Von Willebrand Factor. From the last 40 years Child Pugh Turcottee score has been used for assessing the patient with cirrhosis. It is popular because of its simplicity and can be used at bed side. There are five variables out of which two determinants are based on subjective assessment and other three are objective assessment. According to these five determinants the patients are classified as the child A, child B, child C. Child Pugh score comprise severity and presence of ascites and encephalopathy, prolongation of prothrombin time, level of bilirubin and albumin.

On the bases of points patient are classified into three classes as child A, child B, child C. CPS classification was based on empiric assessment but many studies shown that CPS is predictive assessment in patient with liver disease [4]. MELD for end stage liver disease was introduced in Brazil in 2006 for liver transplantation.

The severity of cirrhosis and mortality are assessed and give priority to transplant liver in patient with more severe condition and also helpful in hepatocellular carcinoma. In united state it was introduced in 2001 and it reduced the mortality rate. This model is helpful in more severe cases of cirrhosis. MELD contain three objective variables serum bilirubin, serum creatinin and prothrombin time expressed as international normalized ratio (INR) [7].

The MEGX is rapid and simple test which can assess the function of liver and widely used for liver transplantation in critical care medicines. It is done after an overnight. It is more discriminatory and it recognizes damage of liver earlier than individual liver function test. It is a useful marker to stratify patient with cirrhosis based on liver. The MEGX found broader application for assessment of hepatic function in transplantation, critical care medicine and various experimental model [9].

Von willebrand factor is released by endothelial cells (vWF-Ag) and it is an indicator of endothelial cells activations. It is important adhesive protein for both adhesive and aggregation. Estimation of vWF-Ag play crucial role in stress, hemostasis. Patient with liver cirrhosis, increase level of vWF-Ag So, it play important role as marker for prediction of varices, portal hypertension and mortality in patient with liver cirrhosis [12].

All these four scores are used to detect the severity or stage of liver disease and help to detect the survival rate of the patient or either stage of the patient. Child Pugh score is too old method for prediction but is more accurate for detecting the liver condition then the others ones. After the introduction of MELD score as priority need for liver transplantation, the increase in the number of transplantation of patient for hepatocellular carcinoma was observed. The patient with advanced cirrhosis were also done and there is decrease in complication after the transplantation and there was no change in the 3 month and 1 year post transplantation survival rate but is not superior to Child Pugh score because of their efficacy in case of liver transplantation. The measurement of vWF-Ag is expected as noninvasive valuable, accessible and affordable for liver cirrhosis and portal hypertension. Potential risks of patient cirrhosis with portal hypertension can easily asses by vWF-Ag level. It could be used to predict the survival rate of patient with cirrhosis independent of Child-Pugh score stages.

The MEGX is more detectable for early damage of the liver than liver function test and confirmed the ability of MEGX to classify each Child Pugh according to specificity and sensitivity. At all point studied both the Child Pugh and MEGX both are correlated. There is increase in the severity of cirrhosis which is identified by decreased in MEGX production [5, 8, 13, 11].

**Epidemiology:** Liver disease (Hepatitis C) is globally dispersed disease and show significant genetic variation over whole world population most affected regions are Africa, central and east Asia. Worldwide the major cause of liver disease is hepatitis C that is the major cause of morbidity and mortality [1]. Internationally prevalence that, 170 million peoples having hepatitis C and estimated 500000 were died in 2010 due to hepatitis C. The epidermiological data based on complexicity and uncertainty that related to geographical dispention of hepatitis C.

The defining of associated risk factors and evaluation of cofactors that increase its progression. This estimate is on weight averages for region than individual countries, due to lack of proper data in many countries. It may judge that approximate HCV accounts for 27% of cirrhosis and 25% of hepatocellular carcinoma. The major mode of transmission above various countries is sharing drug injection equipments.[2] Where as the incidence of HCV on worldwide is not known, because the acute infections are generally asymptomatic and is difficult to differentiate it. The prevalence rate of hepatitis C in United state, Europe and India are mentioned in the (**Table 1**) where as incidence rate of hepatitis C in United state, Western Europe, Japan are mentioned in (**Table 2**). Hence the incidence and prevalence rate define the occurrence of previous and newly cases of hepatitis C in mainly developed countries [3]. Rest from these 25% symptomatic, 60-80% have chronic liver disease and 20% have cirrhosis. 5-7% died due to critical infection [3]. So various scores are used to overcome this situations.

**TABLE 1: PREVALENCE RATE OF LIVER DISEASE (HEPATITIS C) IN SOME COUNTRIES** [3]

| Countries | Prevalence Rate |
|---|---|
| United state | 2-4 million |
| Europe | 5-10 million |
| India | 12 million |

**TABLE 2: INCIDENCE RATE OF LIVER DISEASE (HEPATITIS C) IN SOME COUNTRIES** [3]

| Countries | Incidence Rate (New Cases) |
|---|---|
| United state | 1,50,000 |
| Western Europe | 1,50,000 |
| Japan | 3,50,000 |

## METHODS:

**Child Pugh Score:** Child Turcotte Pugh score has been used from the last 40 years for assessing the prognosis of cirrhosis. CTPS classification is the most widely applied and reported system as it is used at the bedside [1]. It include the presence and absence or the severity of ascites, encephalopathy and change in the INR ratio and level of albumin and bilirubin. Points are ranges from 5-15 and on the basis of these points the patients are arranged into three child classes. In child A it ranges from 5-6, in child B it range from 7-9 and in child C it ranges from >9. Hence it is divide as low, intermediate and poor risk patient. CTPS has been proved over many years in studies but recently it has been challenged because of encephalopathy and ascites are subjective variables with interobserver variance.

As well as the maximum effect of the CTPS score, various studies demonstrate that CTPS is predictive tool in assessing the patient with liver disease and each of the five clinical variables of individual and their classification had prognostic significance [4].

**Scoring:** It includes 5 clinical parameters which measure the severity of liver disease mentioned in (**Table 3**). It was invented by Dr. C.G. Child and Dr. J.G. turcotte of the University of Michigan in 1964 and was modified in 1972.

The adding up of these scores will define the class of CTPS (severity of disease) and their survival rate either 1 year survival or 2 year survival mentioned in (**Table 4**) [5]. CTPS is better for predicting short term mortality in patient with liver disease and better than MELD for predicting morbidity. But it has limitations also as it include two subjective predictive value. Many studies have shown that CTPS is predictive in assessment of prognosis of liver diseased patient.

These studies demonstrate that each of five clinical parameters and over all CTPS classification had prognostic importance. The difficulties and interobserver variability for the subjective parameter in the CTPS give rise to search of another scoring system which had better predictive markers and is more objective then CTPS [5, 6].

**TABLE 3: CHILD TURCOTTE PUGH SCORE** [5]

| Parameter | Points | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| Encephalopathy | None | Grade 1-2 (or suppressed with medication) | Grade 3-4 (or refractory) |
| Ascites | None | Mild/ Moderate | Severe |
| Serum Bilirubin (total) (mg/dl) | <2 | 2-3 | >3 |
| Albumin (g/dl) | >3.5 | 2.8-3.5 | <2.8 |
| PT (sec prolonged) | <4 | 4-6 | >6 |
| or INR | <1.7 | 1.7-2.3 | >2.3 |

**TABLE 4: POINT SCORES ARE THEN ADDED UP AND CLASSIFIED AS** [5]

| Points | Class | 1 Year Survival | 2 Year Survival |
|---|---|---|---|
| 5-6 | A | 100% | 85% |
| 7-9 | B | 81% | 57% |
| 10-15 | C | 45% | 35% |

**MELD (Model for End Stage Liver Disease):** Model for end stage liver disease was introduced in 1999 for better prediction of risk of mortality and morbidity in liver diseased patient as well as determination of liver transplantation priorities. MELD includes all the objective parameters as INR (International Normalized Ratio), bilirubin, serum creatinine and is calculated with statistically derived coefficient logarithmic transformation and require software for their multiplication on a scale with no upper and lower limits. Hence various drawbacks of the Child Pugh score is avoided [7].

MELD Score = {0.957* ln(Serum Cr) + 0.378* ln (Serum Bilirubin) + 1.120* ln(INR) + 0.643} * 10 (if hemodiaysis, value for creatinine is automatically set to 4.0).

The range of MELD score is from 8 to 40. 8 is considered to be slighter ill and 40 represent the severely ill. The four levels of MELD according to their range are mentioned in (**Table 5**) [8].

**TABLE 5: NEED OF THE LABORATORY TEST ACCORDING TO THE RANGE** [8]

| Range | Need Lab Test |
|---|---|
| Greater than or equal to 25 | every 7 days |
| 24-19 | every 30 days |
| 18-11 | every 90 days |
| Less than or equal to 10 | every year |

It is preferred over CTP because it includes all objective variables. MELD was initially designed for patients of transjugular interahepatic portasystemic shunts (TIPS), in order for liver transplant allocation in patient with decompensated liver cirrhosis. But nowadays MELD mainly use for the survival prediction in all patients to predict whether patient is undergoing for transplant or not [4]. The benefits of MELD over CPS are all the parameters are objective and not influenced by the external factors, according to proper prognosis each variable is influenced, it is continuous and for large population and is based on statistical analysis. Although it has some limitations as not properly defined. Cut-off values for classifying patient, not proper validation in some clinical trials and need of calculation [8].

**MEGX (Monoethylglycinexilidine):** In human liver lignocaine is metabolized to Monoethyl-glycinexilidine as a metabolite. After the intravenous injection of lignocaine concentration of MEGX in plasma is measured many time in 0 - 30 minutes, but this test had done after an overnight fast. The concentration of MEGX was determined by high performance liquid chromatography with UV detection. There is decrease in MEGX concentration in abnormal liver function. Its increase concentration define the normal functioning of liver.

It is rapid and simple test which can assess the functioning of liver and widely used for liver transplantation in critical medicines care. It is more discriminatory and it recognized damage of liver earlier than individual liver function test. It is useful marker to stratify patient with cirrhosis based on liver. The MEGX found broader application for assessment of hepatic function in transplantation, critical medicine care. The test value for MEGX from 15-30 minutes is less than 10 microgram/l (poor 1 year survival rate) [9].

As CTPS is the basis of prognostic evaluation of liver disease patient but MEGX test may be a complement to the various score when patient is being identified for liver transplantation. In prediction of one year or six month mortality in child B (CTPS). MEGX is the best tool. Impaired metabolic activity and impaired blood flow in cirrhotic patient is reflected by MEGX. This test represent load stress test and is influenced by hepatic blood flow while it is expression of residual metabolic activity. But this test is not superior to child pugh in term of identifying the stage of liver disease or hepatitis C. The ability of MEGX test to arrange each class of child-pugh score is confirmed by receiver operating characteristics (ROC) analysis with high sensitivity and specificity. At all the time point studies these two scores are correlate with each other [10, 11].

**Von Willibrand Factor:** It is non invasive and simple method to detect various liver related problems like cirrhosis, portal hypertension, decompensation, mortality and predict different stages of fibrosis. It is an antigen released from activated endothelium and is elevated in liver diseased patient. Its value can also determine the compensated and decompensated liver cirrhosis and it act as marker in prediction of mortality [12]. It is a type of adhesive protein for platelets aggregation and adhesion. Any dysfunction in endothelium is due to increased intrahepatic vascular resistance in liver cirrhosis. It is released by activated endothelial cell and is an indicator of endothelial cell injury and thrombocytes activation, which leads to platelets aggregation and thrombotic events. This resulted in portal pressure increment and might be worsening of fibrosis.

Depending on primary Haemostatic, it has important role in high shear stress, vascular disease, increase hepatic vascular tone of cirrhotic liver. It is also a risk factor in heart disease like myocardial infarction and angina pectoris.

It's plasma level is checked in laboratory with fully automated Simultaneous thermal analyser (STA) earlyanalyser and vWF-liatest. Normal range of von willebrand factor is 30-50 IU/dl. Its cut off value at 315% can classify compensated and decompensated liver cirrhosis patient with survival. With increase in CTPS the vWF level increases and also predict response to antiviral therapy. So vWF has potential to add with clinically relevant therapeutic and diagnostic algorithms for liver cirrhotic patient. It also helpful in predicting subclinical cirrhosis in hepatitis C. It is also used with CTPS but have no relation with MELD and MEGX. Although they all are performed due to same purpose [13].

**CONCLUSION:** It conclude that as HCV is asymptomatic when it is in treatable stage, so proper awareness about it. Its screening should be done to prevent the incidence of disease. Child pugh score is very sensitive score in estimating the future prognosis of liver disease and its stages. As it is more easy to perform at bedside and stratify patient undergoing liver diseases like hepatitis, cirrhosis *etc*. CTPS is better indicator for inpatient mortality as well as prolonged hospitalized patient. It is important and traditional component for evaluation of liver diseased patient but with various short coming such as some objective parameters are not involved. But MELD is for predicting short term mortality. It is more objective but it is not superior than CTPS. It is for predicting the survival rate in liver transplantation. It is also very sensitive score for estimating future prognosis of liver disease.

Monoethylglycinexylidine is best tool. It competent to the various score when patient is being identified for liver transplantation as it is very useful marker in impaired metabolic activity and blood flow in cirrhotic patient. But MEGX is not superior to CPS to identifying stages in various liver disease. Von willibrand factor is a new non invasive method for predicting the survival rate of patient with compensated and decompensated liver cirrhosis, also a good marker for mortality and for staging the patient with liver cirrhosis with hepatitis C. It is simple to detect various liver related problems like cirrhosis, portal hypertension, mortality and predict different stages of fibrosis. As from all four, CTPS is the basis of prognostic evaluation of liver disease but all other are competent to various score to identify patient with liver disease with different complications. These all are done to estimate the stage of disease and survival rate of diseased paitent and preventive measure are taken to overcome the disease and to prevent the severity of disease.

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