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Evaluation of the Relationship Between MELD Score and Portal Vein Thrombosis (PVT) in Patients with Liver Cirrhosis

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Abstract

Introduction: Portal vein thrombosis is one of the most important complications of cirrhosis, which is associated with hepatocellular carcinoma. As portal vein thrombosis (PVT) can be a major cause of death in cirrhosis patients, especially those who are waiting for transplantation, its early diagnosis and timely treatment are necessary. The objective of this research was to evaluate the relationship between MELD Score and development of cirrhosis and portal vein thrombosis.Methodology: In this cross-sectional research, patients with liver cirrhosis admitted to Imam Khomeini Hospital in Urmia were evaluated. After performing Color Doppler sonography of portal vein, the MELD Score of patients was calculated and the obtained data were analyzed using SPSS 20 software.Results: In this research, 103 patients with liver cirrhosis hospitalized in the internal units of Imam Khomeini Hospital in Urmia were evaluated. Out of these patients, 20.4% had portal vein thrombosis and 79.6% had no portal vein thrombosis. In the MELD Score classification into two groups of less than 13 and more than 13, portal vein thrombosis in the first group (less than 13) was 28.6% and in the group of more than 13, it was 71.4%. The results revealed that with increasing MELD Score more than 13, the percentage of patients with portal vein thrombosis increases, and portal vein thrombosis is significantly associated with MELD Score above 13.Conclusion: owing to development of thrombosis in lower MELD Scores and the possible effects and complications of liver disease development following liver vein thrombosis, we should not wait for higher MELD Score in follow up of these patients and the patients should be diagnosed and treated timely.

Keywords: Cirrhosis, MELD Score, Child Score, Portal Vein Thrombosis.

Introduction

The liver is the main source of metabolism of three important nutrients, including protein, fat and carbohydrates. Cirrhosis is caused by various mechanisms of liver damage leading to necroinflammation and fibrosis (Nishikawa H, Osaki, 2015) Cirrhosis is a common disease associated with high morbidity and mortality and most patients are irreversible. In the uncompensated cirrhosis, portal hypertension, bleeding caused by esophageal varices, ascites, jaundice, coagulation disorders and encephalopathy and portal vein thrombosis are seen (Jiang et al., 2010; Ahmad et al., 2007; Durand & Valla, 2005). Portal vein thrombosis is one of the most common complications of cirrhosis associated with hepatocellular carcinoma (Webster et al., 2005). Portal vein thrombosis (PVT) is rarely seen in the general population, but it is seen more in patients with liver cirrhosis, and its prevalence increases with increasing severity of the disease (von et al., 2017; Mantaka et al., 2018). Portal vein thrombosis (PVT) occurs by interrupting in normal blood flow in portal vein due to blood clotting. Thrombophilia conditions, abdominal inflammation, tumor attack, and liver cirrhosis are among the most common causes of portal vein thrombosis (PVT) (Rottenstreich et al., 2017; El Lakis et al., 2017).

The imbalance of the hemostatic mechanism (both protein and anticoagulant agents) is involved in the development of thrombosis and finally portal vein thrombosis (PVT). The incidence of portal vein thrombosis (PVT) is seen more in developed stages of cirrhosis (Yamashita et al., 2014). Portal vein thrombosis can occur in outer and inner parts of the venous region and lead into mesenteric vein or chest vein (Tsochatzis et al., 2010). The incidence of portal vein thrombosis (PVT) varies depending on age, liver diseases, portal vein blood flow rate, and its anticoagulant status (Nery et al., 2015). The rate of incidence of portal vein thrombosis in patients with cirrhosis is unknown, but the mean prevalence of 16% has been reported in this regard. As portal vein thrombosis can be a major cause of death in patients with cirrhosis, especially those wait for transplantation, its early diagnosis and timely treatment are essential. Much information

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has been obtained about the causes of this disorder over the recent years. Male gender, previous abdominal surgery, encephalopathy, ascites, history of varices bleeding, thrombocytopenia, and Child C class have been reported as factors susceptible to portal vein thrombosis in people with cirrhosis (Amitrano et al., 2004; Francoz et al., 2005).

Evaluation of the severity of disease is essential in control of developed liver patients and a method predicting the mortality and disability in developed liver disease should be used (Al Sibae & Cappell, 2011; Londoño et al., 2006; Kalabay et al., 2007). The Meld scoring system is a valid method to determine the severity of the disease. MELD Score is calculated based on three biochemical variables including INR, bilirubin, and creatinine (Kalabay et al., 2007). The symptoms of portal vein thrombosis are very heterogeneous, and in many cases, it may be associated with severe complications caused by intestinal infarction or varicella bleeding. Thus, the prognosis and treatment of portal vein thrombosis depends on the location, degree of expansion rate of growth as well as the risk factors for thrombosis and the stage of developed liver disease (Jiang et al., 2010). The objective of this research was to evaluate the relationship between MELD score and development of portal vein thrombosis and determine the frequency of portal vein thrombosis in patients with liver cirrhosis based on age and gender.

Methodology

In this cross-sectional research, patients with liver cirrhosis admitted to Imam Khomeini Hospital in Urmia were evaluated. Patients' medical records were first measured in terms of MELD score, that is, three laboratory parameters (creatinine, bilirubin and INR), and age of patients, and MELD Score calculator and the up-to-date software 21.6 were calculated. Patients in this group were selected who underwent Color Doppler sonography examination in terms of portal vein thrombosis. Patients without these examinations were excluded. It should be noted that Color Doppler sonography and all patient tests were performed at Radiology and Imam Laboratory of Khomeini Hospital. Finally, the data were analyzed using SPSS20 software.

Results

In this research, a total of 103 patients were examined, which 21 (20.4%) of them had portal vein thrombosis and 82 (79.6%) of them were without portal vein thrombosis. Out of 82 patients without venous thrombosis, 43 (52.4%) were male and 39 (47.6%) were female. Out of 21 patients with portal vein thrombosis, 13 (61.9%) were male and 8 (38.1%) were female. Based on the Chi-square test, there was no significant difference between the gender of the patients and the presence of portal vein thrombosis ($P = 0.29$). The mean age of patients with portal vein thrombosis was 55.76 ± 17.13 and in patients without portal vein thrombosis, it was 59.69 ± 16.36 years. Based on the t-test, there was no significant difference between the age of patients and presence of absence of portal vein thrombosis ($P = 0.77$). Of the 21 patients with portal vein thrombosis, 1 patient (4.8%) was in age group of less than 30 years old and 20 patients (95.2%) aged over 30 years.

Out of 82 patients without portal vein thrombosis, 2 (2.4%) patients were in the age group of less than 30 years old and 80 (97.6%) aged over 30 years. Based on the Fisher Exact test, there was no significant difference between the age of patients and the incidence of portal vein thrombosis ($P = 0.44$). The mean MELD score was 17.66 ± 6.35 in patients with portal vein thrombosis and 16.30 ± 6.72 in patients without portal vein thrombosis. Based on the T-test, there was no significant difference between the mean MELD scores in patients with and without portal vein thrombosis ($P = 0.40$). Out of 21 patients with vein thrombosis, 6 patients (28.6%) had a MELD score less than 13 and 15 patients (71.4%) had MELD score over 13. Out of 82 patients without portal vein thrombosis, 24 (29.3%) had a MELD score less than 13, and 58 patients (70.7%) had a MELD score over 13.

Based on Fisher Exact test, there was no significant difference between MELD scores in patients with and without portal vein thrombosis ($P = 0.45$). Out of 21 patients with portal vein thrombosis, 6 patients (28.6%) had MELD Score less than 13, and 8 patients (38.1%) had MELD Score between 13 and 20, and 7 patients (33.3%) had MELD Score more than 20. Out of the 82 patients without portal vein thrombosis, 24 patients (29.35%) has MELD score less than 13, and 39 patients (47.6%) had MELD Score between 13-20 and 19 patients (23.2%) had MELD score more than 20. Based on Chi-square test, there was no significant difference between the MELD scores of patients with thrombosis or thrombosis ($P = 0.62$). CHILD Score in 21 patients with portal venous thrombosis was as follows: it was score A in 5 patients (23.8%), score B in 6 patients (28.6%), and score C in 10 patients (47.6%). CHILD Score in 82 patients without portal vein was as follows: score A in 22 patients (26.8%), score B in 27 patients (32.9%) and score C in 33 patients (40.2%). Based on the Chi-square test, there was no significant difference between the CHILD Scores of patients with and without portal vein ($P = 0.82$).

In examining the gender of patients in terms of having association with portal vein thrombosis in our two groups, in patients with venous thrombosis, out of 13 patients with portal vein thrombosis, 3 (21.1%) had a MELD score of less than 13, 6 patients (46.2%) had MELD Score between 13-20, and 3 patients (37.5%) had MELD score higher than 20%, and out of 8 female patients with portal vein thrombosis, 3 (37.5%) had MELD Score less than 13, 2 patients (25%) had MELD Score between 13-20 and 3 patients (37.5%) had MELD Score over 20. Based on Chi-square test, there was no significant difference between the MELD Score and the gender of patients

(P = 0.66). In patients without venous thrombosis, out of 43 male patients, 9 patients (20.9%) had MELD Score less than 13, 23 patients (53.5%) had MELD Score between 13 and 20, and 11 patients (25.6%) had MELD score higher than 20 and out of 39 female patients, 15 patients (38.5%) had MELD Score less than 13, 16 patients (41%) had MELD Score between 13-20 and 8 patients (20.5%) had MELD score over 20. According to Chi-square test, there was no significant difference between the MELD Score and gender of patients (P = 0.21).

The results of this research revealed that there is a significant correlation between MELD Score and CHILD Score based on Pearson correlation coefficient (R = 0.68 and P = 0.001) (Table 1).

Table 1: Pearson Correlation Coefficient with MELD Score and CHILD Score

Variable	Pearson Correlation Coefficient	P-value
CHILD Score and MELD Score	0.68	0.001

Based on correlation coefficient, a statistical analysis between two scores showed that in patients with portal vein thrombosis, in patients with MELD Score less than 13, 3 patients (50%) had Child score A and 3 patients (50%) had Child score B. Out of 8 patients with MELD Score of between 13 and 20, 2 patients (25%) had Child Score A, 3 patients (37.5%) had Child Score B and 3 patients (37.5%) had Child Score C. In patients with MELD Score of over 20, 7 patients had Child Score C. According to Chi-square test, there was no significant correlation between CHILD Score and MELD Score (P = 0.001) (Table 2).

Table 2: Distribution of absolute and relative frequency of MELD group given CHILD in patients with and without portal vein thrombosis

portal vein thrombosis	Group MELD	CHILD			Total
		A	B	C	
Yes	Less than 13	3 (50%)	3 (50%)	0 (0%)	6 (100%)
	13-20	2 (25%)	3 (37.5%)	3 (37.5%)	8 (100%)
	Over 20	0 (0%)	0 (0%)	7 (100%)	7 (100%)
Total		5 (23.8%)	6 (28.6%)	10 (47.6%)	21 (100%)
thrombosis yes	Group MELD	CHILD			Total
		A	B	C	
No	Less than 13	14 (58.3%)	9 (37.5%)	1 (4.2%)	6 (100%)
	13-20	7 (17.9%)	15 (38.5%)	17 (43.6%)	39 (100%)
	Over 20	1 (5.3%)	3 (15.8%)	15 (78.9%)	19 (100%)
Total		22 (26.8%)	27 (32.9%)	33 (40.2%)	82 (100%)

In the laboratory studies, the mean INR was 1.79 ± 0.76 in patients with portal vein thrombosis and 1.78 ± 0.69 in patients without portal vein thrombosis. Based on T-test, there was no significant difference between the level of INR in patients with and without portal vein thrombosis (P = 0.95). The mean PT was 17.35 ± 4.09 in patients without portal vein thrombosis and 17.29 ± 3.58 in patients with portal vein thrombosis. Based on T-test, there was no significant difference between PT levels in patients with and without portal vein thrombosis (P = 0.94). The mean bilirubin was 3.85 ± 0.45 in patients with portal vein thrombosis and 3.85 ± 0.44 in patients without portal vein thrombosis. In addition, there was no significant difference between the levels of bilirubin in patients with and without venous thrombosis (P = 0.71). The mean albumin was 2.92 ± 0.88 in patients with portal vein thrombosis and 3.47 ± 3.5 in patients without portal vein thrombosis. There was no significant difference between the levels of albumin in patients with and without venous thrombosis (P <0.51).

In examining the underlying causes of patients and their possible association with portal vein thrombosis in patients with liver cirrhosis who had port vein thrombosis, 9 patients had underlying disease of hepatitis B, and cryptogenetic reason as reported in medical records of rest of the patients, that is, 42% of patients had hepatitis B and 58% of them had cryptogenetic causes. In patients with liver cirrhosis who did not have thrombosis, in addition to cryptogenetic cause, 6 other causes were reported (Table 3).

Table 3: Frequency distribution of causes of underlying diseases in patients without portal venous thrombosis

	Absolute frequency	%
Hepatitis B	16	19
Autoimmune Hepatitis	3	0.3
Hepatitis C	4	0.4

PBC (Primary Biliary Cirrhosis)	2	0.2
Hemochromatosis	1	0.1
Alcoholism	1	0.1
Cryptogenic	55	69

In the thrombosis group, 4 female and 5 male had hepatitis B, and in the non-thrombosis group, out of 16 patients with hepatitis B, 10 were male and 6 were female. In both groups, hepatitis B was more common in males than that in females.

Discussion and Conclusion

The liver cirrhosis represents the final stage of the chronic liver disease, and has a range of clinical manifestations and complications, which some of them can cause mortality (Chang et al., 2015; Fujiyama et al., 2017). Different biochemical parameters such as serum bilirubin, albumin, creatinine, as well as encephalopathy and ascites are the main predictors for survival of patients with liver cirrhosis (Fujiyama et al., 2017; Kamath & Kim, 2007). Portal vein thrombosis (PVT) is a serious problem in patients with cirrhosis requiring a dynamic management approach. There is uncertainty about the clinical importance of portal vein thrombosis in the cirrhosis population, since portal vein thrombosis data are usually derived from retrospective studies and small cohorts (Loudin & Ahn, 2017). In this research, 20.4% of the subjects suffered portal vein thrombosis, which is in line with that of the study conducted by Abdel-Razik et al in Egypt in 2015, as they reported the percentage of portal vein thrombosis 17.9% in patients with liver cirrhosis (Abdel-Razik et al., 2015). In another study conducted by Chen H et al in 2014 in China, the incidence of portal vein thrombosis was 24.7% and 85% of patients with hepatitis B and patients with Child B and C included the highest percent of patients with portal vein thrombosis. These results are in line with those of our study, which showed the highest percentage of patients with portal vein thrombosis was Child C and then Child B. In our research, 47.6% of patients with portal vein thrombosis was Child C and 28.6% was Child B and 28.8% was Child A (Chen et al., 2014). The underlying cause of liver cirrhosis and its possible association with liver vein thrombosis were also studied. The most common cause of disease was cryptogenetic accounted for about 69% of patients. However, the second underlying cause of the disease was hepatitis B, which due to the more prevalence of hepatitis B in Iran, it accounts for 26% of the underlying disease in this study for liver cirrhosis. Other causes included chronic hepatitis, hepatitis C, autoimmune hepatitis and other causes, such as PBC (primary bile cirrhosis) and hemochromatosis and alcohol, and so on .Statistics of western countries suggest that hepatitis B was the most common underlying cause. Only one alcohol hepatitis was found in this research. The prevalence of hepatitis B was 42.8% in portal vein thrombosis group. However, it was 42.8% in the non-thrombosis group. In this study and in the study conducted by Chen in China, hepatitis B was the main cause of cirrhosis (Chen et al., 2014).

In our study, the mean MELD Score was 16.79 ± 7.52. The mean MELD Score was 17.66 ± 6.35 in patients with portal vein thrombosis and it was 16.57 ± 6.58 in patients without portal vein thrombosis, but there was no significant difference between the mean MEDL Scores in these two groups. However, the results show that the mean MELD Score was more in patients with portal port vein thrombosis than that in patients without thrombosis with difference of 1.09. In a research conducted by Hernández Conde et al., the mean MELD score was obtained 15 in both groups and MELD Score was obtained 16.6 in patients with portal vein thrombosis and 14.9 in patients without portal vein thrombosis, indicating that MELD score is higher in patients with portal vein thrombosis. Moreover, the results of this study showed that portal vein thrombosis is correlated with higher mortality in the first 30 days (Hernández et al., 2016). However, in another study conducted by Qi et al, they reported that mortality in patients with cirrhosis in a hospital with portal vein thrombosis was not significantly different from that in patients without portal vein thrombosis (Qi et al., 2016). However, as we considered two types of classification in terms of the specific number for MELD score, in the patients with cirrhosis with portal vein thrombosis, 28.6% had MELD score below 13% and 71.4% had MELD score greater than 13%.

It seems that portal vein thrombosis to develop in even lower MELD scores, but its prevalence is more in moderate and moderate to high MELD scores. According to our statistics, by increasing MELD score from 13, it increases from 28.6% to 71.4%. It is assumed that portal vein thrombosis to be associated with an increase in MELD in patients, especially with a MELD more than 13. However, this association cannot be stated with specific number in these types of studies conducted on low sample size, since different results might be achieved in studies with larger sample size. It can be stated that Child C is the most common for portal vein thrombosis. In our research, according to Pearson correlation coefficient, there is a significant correlation between MELD Score and CHILD Score ($R = 0.68$ and $P = 0.001$) and the results of examining the CHILD Score in 21 patients with portal vein thrombosis, it was Score A in 5 (23.8%) people and Score B in 6 patients (28.6%) and Score C in 10 people (47.6%). This investigation showed that MELD Score increases as the CHILD Score increases and this relationship can predict the liver cirrhosis and increase the complications, including bleeding.

Recommendations

As portal vein thrombosis can occur at varying levels in patients with liver cirrhosis with different MELD scores (low-moderate-high), it is recommended further studies to be carried out on higher number of patients and prospective studies are recommended to be conducted

to follow-up the liver cirrhosis patients in terms of portal vein thrombosis in order to achieve more accurate, different, and more applied results.

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