Incidence of Venous Thrombosis among Cirrhosis Patients and Study of Risk Factors Contributing to 90 Day Mortality

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ABSTRACT

BACKGROUND

Chronic liver disease causes an imbalance in the coagulation system, but available data on liver disease and risk of venous thrombosis are conflicting. Clinical studies are therefore needed to understand the prevalence and risk factors associated with mortality to decide appropriate care of these patients. We studied the incidence of venous thrombosis in three CTP (Child-Turcotte-Pugh) class of cirrhotic patients and associated risk factors predicting 90-day mortality.

METHODS

A cross sectional observational study of one-year duration was conducted at a tertiary-care teaching hospital among patients admitted with chronic liver disease. 150 hospitalised patients with cirrhosis were enrolled and followed up for 3 months. Incidence of thrombosis was recorded in different CTP subclass. Three-month mortality rates in different subgroups were compared by using normal test of proportions. The association between types of thrombosis and CTP class of liver cirrhosis was studied using Mann-Whitney U test, a non-parametric test. Mortality association with various parameters was evaluated using non-parametric test. P-value of ≤ 0.05 was considered significant.

RESULTS

Incidence of venous thrombosis in cirrhotic patients was 4 % in this study. Association of thrombosis with various clinical parameters and different CTP subclass was statistically non-significant. During the 3-months follow-up 24 patients died. Deceased had higher CTP score (mean CTP score - 9.58) as compared to survivors (mean CTP - 8.48) (P-value 0.049). Presence of ascites (P-value 0.037), higher serum urea (P-value 0.001), creatinine (P = 0.004), and total leucocyte count (P = 0.008) were significantly associated with mortality.

CONCLUSIONS

Thrombosis in chronic liver disease (CLD) especially portal vein is common and presents a therapeutic challenge as these patients are also at increased risk of bleeding. Higher CTP score, serum creatinine, leucocyte count and presence of ascites in CLD patients at admission are poor prognostic markers.

KEYWORDS

Deep Venous Thrombosis, Chronic Liver Disease, Cirrhosis, Thrombosis, Portal Vein Thrombosis

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BACKGROUND

Coagulopathy and thrombocytopenia are often present in cirrhotic patients[1] and it is assumed that they have a reduced risk for venous thrombosis.[2] Patients with cirrhosis have protein synthesis dysfunction causing deficiency of procoagulant clotting factors. This may result in some level of endogenous coagulopathy. Elevated level of international normalized ratio (INR) may further lead to the assumption of low risk of thrombosis in these patients.

Thus, cirrhotic patients were believed to be the state of auto anticoagulated. However, despite an elevated prothrombin time and INR, thrombotic events have been documented in cirrhotic patients. Recently there has been growing concern regarding increase risk of thrombotic complications as well.[3] Prevalence rate of portal vein thrombosis is 10 % - 25 % in patients with liver cirrhosis and it further rises with severity of disease.[4,5,6] Emerging evidence suggest occurrence of non-splanchnic venous thromboembolic events (VTE) in these patients, mostly lower extremity deep vein thrombosis (DVT) and pulmonary embolism.[7,8]

Liver disease attributes huge health and economic burden. Health care of these patients constitutes approximately 1 % of the total national health expenditure of United states.[9] Venous thromboembolic events with cirrhosis is associated with increased length of hospital stay,[10,11,12] hospitalisation cost[13] and mortality as well.[10] There is an evolving pathogenesis suggested by various studies that hypercoagulation state causes hepatic microthrombi, resulting ischemic changes activate hepatic stellate cells which subsequently lead to progression of fibrosis.[14,15,16,17]

Further a recent study suggests that prophylactic enoxaparin therapy decreases the risk of decompensation in cirrhosis, provides additional support to this concept.[18] Knowledge of the derangement of haemostatic pathways in cirrhotics thus, has become more significant. This is important not only to predict the bleeding or thrombotic complications, but also for the therapeutic opportunity to manipulate the natural course of the disease.[15]

Northup et al. demonstrated a lower incidence of venous thromboembolism (VTE) in cirrhosis patients (0.5 %) in contrast to a population-based case control study done in Denmark by Søgaard et al.[19] Thus, prevalence of venous thromboembolism among cirrhosis patients has conflicting results. Further these studies were limited in their ability to identify risk factors for venous thromboembolism. Given these contradictions between the earlier belief of coagulopathy in chronic liver disease and the new evidence suggesting a procoagulant state in these patients, it is important to collect further data to help understand the nature of coagulopathy in chronic liver disease and select patients those would benefit from thromboprophylaxis. Hence, we conducted a cross sectional study to find the incidence of venous thrombosis in three CTP (Child-Turcotte-Pugh) class of cirrhotic patients and associated risk factors predicting 90-day mortality.

METHODS

It was a cross sectional observational study conducted on patients admitted with chronic liver disease in the Department of General Medicine, at a tertiary teaching hospital in North India. Patients were enrolled from May 2018 to June 2019.

Sample Size

The prevalence of systemic venous thrombosis has been reported in various studies with conflicting results, ranging between 0.5 % to 1.8 %. The prevalence of portal / splanchnic venous thrombosis was reported to be between 0.6 % to 26 % with increasing incidence in more advanced cirrhosis patients. In view of both these statistics, sample size was calculated on the basis of an anticipated 10 % prevalence of thrombosis in liver cirrhosis, assuming 95 % confidence interval and 10 % permissible error. The optimum sample size thus calculated was 38. The sample size was further increased to include a 20 % non-response to follow up. The final sample size was 50 under each category of CTP score A, B and C thus a total of 150 subjects were enrolled.

Inclusion Criteria

- Patients with cirrhosis of liver based on clinical, laboratory, radiological and endoscopy / elastography evidence.
- Age > 18 years.

Exclusion Criteria

- Patients with history of venous thrombosis.
- Patients with active malignancy.
- Patients with recent major surgery (abdominal or pelvic surgery in the last 4 weeks).
- Patients with paralysis, paresis, or recent orthopaedic cast
- Pregnant and post-partum (up to 12 weeks) patients.

All 150 enrolled patients of liver cirrhosis were divided into 3 classes: A, B and C based on CTP score. Doppler ultrasonography of abdomen and lower limbs was done to look for thrombosis in various vascular beds. Associated clinical, laboratory parameters were assessed at enrolment and thereafter as and when clinically indicated. Patients were followed up to 3 months. In the event of detection of venous thrombosis, patients were started on anticoagulant as per protocol after ruling out contraindications.

Statistical Analysis

The pattern of different types of venous thrombosis was studied by using proportions and percentages. The three-month mortality rates in different subgroups were compared by using normal test of proportions. Patterns of different types of thrombosis were related with the CTP class of

cirrhosis. The significance association of continuous variables was evaluated using Student's t-test. The significance of association between types of thrombosis and CTP class of liver cirrhosis was studied using Mann-Whitney U test, a non-parametric test. Mortality associated with thrombosis was evaluated using a non-parametric test. P-value of ≤ 0.05 was considered significant. The analysis was performed using Statistical Packages for the Social Sciences (SPSS Inc, Chicago, IL, version 22.0 for windows).

Ethical Consideration

A written and informed consent was taken from all subjects. The interventions involved in the present study were completely safe. Personal details of participants were kept confidential. Information regarding the goal of study, the methods being used, the possible outcome were explained. Patient's apprehension regarding discomforts, inconveniences and risks if any were addressed to their satisfaction. The patients were given the right to opt out of the study at any time they want without any impact on the treatment to be given.

RESULTS

There were 84.66 % (127 / 150) males and 15.33 % (23 / 150) females in the study cohort. Mean age of study cohort was 48.39 ± 12.55 with minimum age of 18 years and maximum age of 85 years. Mean duration of hospital stay of study cohort was 6.89 ± 6.47 days. There was no in-hospital mortality in the study cohort.

After discharge 16 % (24 / 150) patients died of complications due to cirrhosis.

A total of 6 patients were found to have thrombosis on Doppler ultrasound in various vascular beds (portal vein-4, mesenteric vein-1 and hepatic vein-1). Out of the 6 patients with thrombosis, 3 patients had alcoholic liver disease, 1 patient had non-alcoholic fatty liver disease (NAFLD), one patient had congestive heart failure with cardiac cirrhosis, and in 1 patient the aetiology of CLD could not be found.

Parameters	Thrombosis (n = 6) (Mean Rank)	Non-Thrombosis (n = 144) (Mean Rank)	Mann Whitney U	P Value
Age (years)	68.42	75.80	389.500	0.683
Platelet count (cells / mm^3)	92.08	74.81	332.500	0.340
TLC (cells / mm^3)	67.42	75.84	383.500	0.642
INR	91.42	74.84	336.500	0.359
Albumin (g / dL)	87.67	74.99	359.000	0.480
CTP score	69.25	75.76	394.500	0.715
Duration of hospital stay (days)	90.33	74.88	343.000	0.390

Table 1. Mean Rank and Respective P-Values of Various Laboratory Parameters in CLD Patients with and without Venous Thrombosis

Parameters	Deceased (n = 24) (Mean Rank)	Survivors (n = 126) (Mean Rank)	Mann Whitney U	P Value
Age (years)	90.19	72.70	1159.500	0.071
Duration of hospital stay (days)	73.88	75.81	1473.000	0.840
Total protein (g / dL)	67.46	77.03	1319.000	0.322
Albumin (g / dL)	62.83	77.91	1208.000	0.116
SGOT (U / L)	86.38	73.43	1251.000	0.181
SGPT (U / L)	87.94	73.13	1213.500	0.126
Urea (mg / dL)	101.33	70.58	892.000	0.001
Creatinine (mg / dL)	98.79	71.06	953.000	0.004
Hb (g / dL)	74.48	75.69	1487.500	0.900
TLC (x 10^3 cells / mm^3)	96.92	71.42	998.000	0.008
Platelet (cells / mm^3)	81.38	74.38	1371.000	0.470
Bilirubin (mg / dL)	78.63	74.90	1437.000	0.701
INR	87.50	73.21	1224.000	0.139
CTP score	91.25	72.50	1134.000	0.049

Table 2. Comparison of Various Parameters and Respective P-Values in Deceased and Survivors Up to 3-Months Follow-Up

Reference	Study Design	Case	Control	VTE %	RR / OR (95 % CI)	Authors Conclusion
Walsh et al.[13] 2013	Case control	27 patients of CLD with VTE	81 patients of CLD without VTE	0.65 (17 out of 2606 admissions)	Low albumin 5.14 (1.05 - 25.2) was assessed as risk factor for VTE	CLD patients with VTE patients had lower AST, ALT, albumin and haematocrit than control group.
Ali et al.[12] 2011	Cross sectional	Cirrhotic patients - 449798		1.80 %	Risk factors for VTE were old age, malnutrition, black race, central venous line placement.	DVT result 25 % increase in length of hospital stay in cirrhotic patient.
Aldawood et al.[11] 2011	Retrospective cohort	Cirrhotic patients - 226		2.7 %		Cirrhotic patients had risk of developing VTE. Suboptimal utilisation of DVT prophylaxis was noted.
Wu et al.[10] 2010	Case control	Compensated cirrhotics = 408253 Decompensated = 241626	Non cirrhotic controls = 575057	0.8 % for cirrhotics,	Age < 45 yr. compensated: 1.23 (1.04 - 1.46) decompensated: 1.39 (1.15 - 1.69) Age > 45 yr. compensated: 0.90 (0.85 - 0.95) decompensated: 0.97 (0.91 - 1.04)	Patients with cirrhosis <45 years of age are at a higher risk for VTE than those without liver disease. In such cases VTE prophylaxis must be considered.
Anthony Lizarraga et al.[20] 2010	Retrospective case control	108 CLD patients with VTE (includes 22 patients with PVT)	108 CLD patients without VTE	0.73 (108 out of 14,790 admissions)		As compared to controls, cases had low haematocrit and albumin, higher aPTT, platelet count and bilirubin.
Dabbagh et al.[21] 2010	Retrospective cohort	190 chronic liver disease patients.		6.3 %		Elevated INR does not appear to be protective against hospital acquired VTE in the CLD setting.
Søgaard et al.[19] 2009	Population based case control	VTE = 99444	Population controls = 496872		Cirrhosis: RR 1.74 (1.54 - 1.95)	There is an elevated risk of VTE in patients with liver disease.
Gulley et al.[7] 2008	Case control	963 cirrhotics	12405 controls	1.87 %	Risk factor for VTE: Albumin 0.47 (0.23 - 0.93) PTT: 0.88 (0.84 - 0.94) multivariate analysis OR 0.87 (0.2 - 2.6)	Cirrhosis not a risk factor on
Northup et al.[8] 2006	Retrospective case control	113 cirrhotics with VTE		0.5 %	Risk factor for VTE: low albumin 0.25 (0.10 - 0.56)	INR, MELD: no correlation

Table 3. Comparison of Various Studies on VTE in CLD

Prevalence of thrombosis in chronic liver disease was 4 %. Various clinical and laboratory parameter frequency were compared in two groups of cirrhosis patients with and without thrombosis as depicted in Table 1. None of the parameters was found to be statistically significant.

In the cohort of 150 patients with chronic liver disease, 24 patients died during the 3-month follow-up period. The mean CTP score was 9.58 ± 2.46 vs. 8.48 ± 2.54 in deceased vs. survivors. Patients with 3-month mortality had higher CTP Score as compared to patient with no mortality (P-value 0.049). In the study 56 % (84 / 150) had ascites, and 44 % (66 / 150) had no ascites on abdominal ultrasound. Among the patients with ascites 20.2 % (17 / 84) patients had mild ascites and 79.7 % (67 / 84) had moderate / gross ascites. Patients with no ascites had a 3-month mortality rate of 7.6 %, patients with mild ascites had 3-month rate of 17.6 %, patients with moderate or gross ascites had a 3-month mortality rate of 23.9 %. Ascites was significantly associated with mortality in the study cohort (P-value 0.037).

Mean urea level in deceased group was 82.5 ± 55.8 mg / dL and mean creatinine was 1.81 ± 0.95. Patients with 3-month mortality (deceased) had significantly higher urea and creatinine levels (P-value < 0.05) as shown in Table 2. There were no statistically significant differences in age, gender, episodes of hepatic encephalopathy, hematemesis, duration of hospital stay, total protein, haemoglobin, platelet count, serum glutamic pyruvic transaminase (SGPT), INR in the study as depicted in Table 2.

DISCUSSION

Chronic liver disease has been predominantly considered to be associated with coagulopathy and bleeding tendencies. More recently it has been discovered that patients with cirrhosis are in a rebalanced state of coagulation with alteration in both pro- and anti-coagulation factors.[22] Though chronic liver disease is associated with increased risk of bleeding, there is increasing evidence to suggest that the risk of thrombosis is not to be discounted in these patients. The present study was aimed at determining the incidence of thrombosis in both splanchnic and non-splanchnic venous beds in patients with liver cirrhosis and identify the associated clinical and laboratory parameters as well as outcomes in cirrhotic patients with thrombosis. Table 3 compares major studies highlighting the risk of venous thrombosis in chronic liver disease. Given the low incidence and prevalence of thrombosis, a retrospective study design was preferred in most studies.

The incidence of thrombosis in this study was 4 % (6 / 150) with 3.33 % for portal vein / splanchnic thrombosis and 0.33 % for non-splanchnic venous thrombosis. There was no de novo thrombosis in the study cohort over a 3 month follow-up period. Portal vein thrombosis is a known complication of cirrhosis. Observation in this study is comparable with systematic review by Aggrawal et al. considering various studies between 2006 to 2013 and reporting an incidence rate of venous thromboembolism from 0.5 % to 8.1 %.[23]

The mean age of patients with thrombosis in this study was 46.0 ± 17.158 years as compared to other studies done by Lizarraga et al.[20] and Northup et al.[8] reported mean age of 56.2 and 54.6 years respectively.

The aetiology of liver disease in this study population was alcoholic liver disease (52 %), hepatitis C (12 %), NAFLD (11.3 %), hepatitis B (6 %) and alcoholic liver disease with hepatitis C (6 %). This was similar to the study by Northup et al.[8] Lizarraga et al.[20] and a multi-centre Indian study by Mukherjee et al.[24] done to delineate the etiological profile of chronic liver disease.

The mean platelet count in patients with thrombosis was higher (137166 cells / mm^3) than that seen in patients without thrombosis (125189 cells / mm^3). This finding although not statistically significant was consistent with findings of the study by Northup et al.[8] and by Lizarraga et al.[20]

The mean INR in this study population with thrombosis vs. non thrombosis was 1.48 ± 0.34 vs. 1.38 ± 0.31, statistically non-significant. A retrospective cohort study by Dabbagh et al. divided cirrhotic patients into 4 INR quartiles, and compared incidence of VTE in the cohort.[24] They found no correlation between incidence of VTE and INR and the risk of VTE was still present even with INR > 2.2. This was also found in the study by Northup et al.[8] where no correlation between higher INR and risk of VTE.

Northup et al.[8] found significant lower serum albumin levels in cirrhotic patients with VTE (2.85 g.dL) than patients without VTE. (3.10 g / dL). The study by Gulley et al.[7] also found low serum albumin to be independently predictive of incidence of VTE. Patients with thrombosis had significantly lower albumin levels than controls in the study by Lizarraga et al. (2.77 vs. 3.49 g / dL).[20] However, the difference of serum albumin between the two groups with thrombosis vs. non thrombosis in this study was not statistically significant.

Patients with thrombosis in the study population were distributed among the three CTP classes. Although our study has limited number of patients with thrombosis, the findings were not indicative of a possible correlation between severity of liver disease and incidence of thrombosis. This was consistent with the findings of the study by Northup et al.[8] where no significant difference was seen in the Model for End-Stage Liver Disease (MELD) scores of patients with thrombosis and patients without thrombosis. Another study by Wu et al.[10] found similar incidence of VTE in patients with or without decompensated liver disease. Portal vein thrombosis is known to be a complication of more advanced liver disease with incidence increasing as liver disease progresses.[25,26] This was not reflected in this study could be because of small number of cases plus this study enrolled other types of non-splanchnic vascular bed thrombosis cases as well. Focused study only on portal vein thrombosis in CLD may be better for this association.

The mean length of hospital stay in the study was 8.67 days in patients with thrombosis and 6.82 in patients without venous thrombosis. This was not statistically significant. This is in contrast to study by Wu et al.[10] and another study by Aldawood et al.[11] stating a significant longer length of hospital stay. Low prevalence due to small sample size could be a limiting factor for this observation.

A study done at a tertiary care centre in North India by Daswani et al.[27] concluded that presence of Child C status and high serum creatinine value (≥ 1.35 mg / dL) accurately predicted 90-days mortality in severe alcoholic hepatitis. Another study done in India by Kumar et al.[28] observed older age, low haemoglobin, higher Child–Pugh Class, spontaneous bacterial peritonitis, and higher serum bilirubin are the independent predictors of in-hospital mortality among cirrhotic patients. This study had similar results for parameters like serum creatinine, CTP score and ascites as in Table 2.

CONCLUSIONS

It is evident in various studies that venous thrombosis does occur in patients with cirrhosis and is associated with significant morbidity. As the life expectancy of patients with cirrhosis increases with improvement in health-care facilities and treatment, the incidence rates of venous thrombosis may increase further. The present study found a 4 % incidence of venous thrombosis in cirrhotic patients. This suggests a need for anticoagulation prophylaxis in patients with cirrhosis. Higher CTP score, serum creatinine, leucocyte count and presence of ascites in CLD patients at admission are poor prognostic markers. Considering the major complication of bleeding in cirrhotic patients, studies evaluating the risk versus benefit of thromboprophylaxis are needed. Large multicentric studies are needed to understand prevalence of thrombosis in various vascular beds, therapeutic and lab monitoring issues in CLD patients.

Limitations of the Study

Due to the low incidence of venous thrombosis in CLD, a prospective study would require a larger cohort over a longer study period to yield significant and accurate results. Also, the low incidence of venous thrombosis in the present study does not allow us to derive meaningful results in relation to various factors. Adequately matched controls would be necessary to define significant associations. While the study did evaluate for DVT, it did not evaluate for pulmonary thromboembolism in the study cohort. A limited follow up period of 3 months may not reflect the true prevalence rates of venous thrombosis as in this study. Patients with venous thrombosis were not evaluated for inherited thrombophilic state as a part of the study. The present study was limited to hospital setting of admitted patients and would not apply to the stable cirrhotic patients in the community.

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REFERENCES

[1] Amitrano L, Guardascione MA, Brancaccio V, et al. Coagulation disorders in liver disease. Semin Liver Dis 2002;22(1):83-96.
[2] Heit JA, Silverstein MD, Mohr DN, et al. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. Arch Intern Med 2000;160(6):809-815.
[3] Tripodi A, Anstee QM, Sogaard KK, et al. Hypercoagulability in cirrhosis: causes and consequences. J Thromb Haemost 2011;9(9):1713-1723.
[4] Tsochatzis EA, Senzolo M, Germani G, et al. Systematic review: portal vein thrombosis in cirrhosis. Aliment Pharmacol Ther 2010;31(3):366-374.
[5] Ponziani FR, Zocco MA, Garcovich M, et al. What we should know about portal vein thrombosis in cirrhotic patients: a changing perspective. World J Gastroenterol 2012;18(36):5014-5020.
[6] John BV, Konjeti R, Aggarwal A, et al. Impact of untreated portal vein thrombosis on pre and post liver transplant outcomes in cirrhosis. Ann Hepatol 2013;12(6):952-958.
[7] Gulley D, Teal E, Suvannasankha A, et al. Deep vein thrombosis and pulmonary embolism in cirrhosis patients. Dig Dis Sci 2008;53(11):3012-3017.
[8] Northup PG, McMahon MM, Ruhl AP, et al. Coagulopathy does not fully protect hospitalized cirrhosis patients from peripheral venous thromboembolism. Am J Gastroenterol 2006;101(7):1524-1528, quiz 1680.
[9] Kim WR, Brown RS Jr, Terrault NA, et al. Burden of liver disease in the United States: summary of a workshop. Hepatology 2002;36(1):227-242.
[10] Wu H, Nguyen GC. Liver cirrhosis is associated with venous thromboembolism among hospitalized patients in a nation- wide US study. Clin Gastroenterol Hepatol 2010;8(9):800-805.
[11] Aldawood A, Arabi Y, Aljumah A, et al. The incidence of venous thromboembolism and practice of deep venous thrombosis prophylaxis in hospitalized cirrhotic patients. Thromb J 2011;9(1):1.
[12] Ali M, Ananthakrishnan AN, McGinley EL, et al. Deep vein thrombosis and pulmonary embolism in hospitalized patients with cirrhosis: a nationwide analysis. Dig Dis Sci 2011;56(7):2152-2159.
[13] Walsh KA, Lewis DA, Clifford TM, et al. Risk factors for venous thromboembolism in patients with chronic liver disease. Ann Pharmacother 2013;47(3):333-339.
[14] Wanless IR, Wong F, Blendis LM, et al. Hepatic and portal vein thrombosis in cirrhosis: possible role in development of parenchymal extinction and portal hypertension. Hepatology 1995;21(5):1238-1247.
[15] Jairath V, Burroughs AK. Anticoagulation in patients with liver cirrhosis: complication or therapeutic opportunity? Gut 2013;62(4):479-482.

[16] Calvaruso V, Maimone S, Gatt A, et al. Coagulation and fibrosis in chronic liver disease. Gut 2008;57(12):1722-1727.
[17] Wright M, Goldin R, Hellier S, et al. Factor V Leiden polymorphism and the rate of fibrosis development in chronic hepatitis C virus infection. Gut 2003;52(8):1206-1210.
[18] Villa E, Cammà C, Marietta M, et al. Enoxaparin prevents portal vein thrombosis and liver decompensation in patients with advanced cirrhosis. Gastroenterology 2012;143(5):1253-1260.e4.
[19] Søgaard KK, Horváth-Puhó E, Grønbaek H, et al. Risk of venous thromboembolism in patients with liver disease: a nationwide population- based case-control study. Am J Gastroenterol 2009;104(1):96-101.
[20] Lizarraga AW, Dalia S, Reinert SE, et al. Venous thrombosis in patients with chronic liver disease. Blood Coagul Fibrinolysis 2010;21(5):431-435.
[21] Dabbagh O, Oza A, Prakash S, et al. Coagulopathy does not protect against venous thromboembolism in hospitalized patients with chronic liver disease. Chest 2010;137(5):1145-1149.
[22] Tripodi A, Primignani M, Chantarangkul V, et al. An imbalance of pro- vs. anti-coagulation factors in plasma from patients with cirrhosis. Gastroenterology 2009;137(6):2105-2111.
[23] Aggarwal A, Puri K, Liangpunsakul S. Deep vein thrombosis and pulmonary embolism in cirrhotic patients: systematic review. World J Gastroenterol 2014;20(19):5737-5745.
[24] Mukherjee PS, Vishnubhatla S, Amarapurkar DN, et al. Etiology and mode of presentation of chronic liver diseases in India: a multi-centric study. PLoS One 2017;12(10):e0187033.
[25] Violi F, Corazza RG, Caldwell SH, et al. Portal vein thrombosis relevance on liver cirrhosis: Italian Venous Thrombotic Events Registry. Intern Emerg Med 2016;11(8):1059-1066.
[26] Amitrano L, Brancaccio V, Guardascione MA, et al. Inherited coagulation disorders in cirrhotic patients with portal vein thrombosis. Hepatology 2000;31(2):345-348.
[27] Daswani R, Kumar A, Anikhindi SA, et al. Predictors of 90-day mortality in patients with severe alcoholic hepatitis: Experience with 183 patients at a tertiary care center from India. Indian J Gastroenterol 2018;37(2):141-152.
[28] Kumar AS, Sibia RS. Predictors of in-hospital mortality among patients presenting with variceal gastrointestinal bleeding. Saudi J Gastroenterol 2015;21(1):43-46.