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Case Report

Management of non-cirrhotic variceal bleeding in pregnant women with Budd-Chiari syndrome in the early second trimester: A case report

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Abstract

Budd–Chiari syndrome is one of the post-hepatic causes of portal hypertension and a potential obstruction causes liver fibrosis. In pregnancy, obstruction of hepatic veins could occur due to stenosis or thrombosis. Variceal bleeding is the most fatal complication in pregnancy with co-existing Budd–Chiari syndrome, with 29.4% incidence of abortion and 33.3% perinatal mortality. The aim of this case report was to present the management of non-cirrhotic variceal bleeding in pregnant women with Budd–Chiari syndrome in the early second trimester. We report a pregnant female at 13–14 weeks gestation presented to the hospital with profuse hematemesis. Doppler ultrasonography (USG) was utilized to confirm the diagnosis of Budd–Chiari syndrome-hepatic vein occlusion type in pregnancy. Abdominal USG revealed hepatomegaly with hepatic veins dilation, while endoscopy showed grade IV esophageal varices and grade IV gastric varices. Laboratory results indicated disseminated intravascular coagulation due to hemorrhage. The patient was given strict fluid resuscitation and three packed red cells transfusion to stabilize the hemodynamic. Bleeding was successfully managed by intravenous octreotide, tranexamic acid, and vitamin K. The case highlights that the management of non-cirrhotic variceal bleeding in pregnancy with Budd–Chiari syndrome requires a multidisciplinary approach and regular fetal monitoring to ensure optimal outcomes.

Keywords: Budd-Chiari syndrome, portal hypertension, variceal bleeding, octreotide, propranolol

Introduction

Budd–Chiari syndrome (BCS) is one of the post-hepatic causes of portal hypertension [1]. Obstruction of hepatic veins eventually will cause liver fibrosis [2,3]. In pregnancy, obstruction of hepatic veins could occur due to stenosis or thrombosis [4]. Women with BCS are at risk of developing severe exacerbation of their underlying disease during pregnancy due to several reasons: elevated blood estrogen level, elevated level of pro-coagulant factors (factors VII, VIII, IX, X, XII, and VWF), low anticoagulants (protein S), reduction in fibrinolysis due to decrease in tissue plasminogen activator (t-PA) activity, increased circulating blood volume, and gravid

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uterus compressing central venous circulation [2,5]. Decompensated cirrhosis in women contributes to maternal risks associated with portal hypertension [6,7].

During pregnancy, significant changes occur in the maternal cardiovascular system, leading to more active blood circulation [2,8]. The resistance in the systemic blood vessels decreases, while the return of blood to the heart, heart rate, and volume of blood pumped per heartbeat (stroke volume) increases [2,7]. As a result, the amount of blood pumped by the heart (cardiac output) can increase by 30% to 40% in the early third trimester [7]. Additionally, the renin-angiotensin-aldosterone system (RAAS) is activated, causing the body to retain fluid, leading to a 45% expansion of plasma volume in the third trimester [2,3,7]. The growing uterus presses on the inferior vena cava [4,6,9]. To facilitate venous drainage during pregnancy, collateral blood vessels, such as the azygos and vertebral veins, and possibly the portal venous system, expand [7]. While previous studies have produced conflicting results regarding the flow of blood in the portal and hepatic veins during pregnancy, more recent data using Doppler ultrasound have shown a 50% increase in portal vein flow in late pregnancy, along with a corresponding increase in overall liver blood flow [2,7,8]. In addition, due to the increased plasma volume, there is a relative normocytic anemia [2,8]. This can lead to a decrease in the platelet count, with approximately 10% of women developing a condition called benign gestational thrombocytopenia in the second or third trimester, where platelet counts range between 100–150 × 10^9 cells/L [7]. Pregnancy also makes the blood more prone to clotting (hypercoagulable state), but it does not affect the international normalized ratio (INR) and prothrombin time (PT) values [7].

Although only a minority of women with BCS become cirrhotic, variceal bleeding can still happen due to portal hypertension [2,10]. Variceal bleeding is the most fatal complication in pregnancy with co-existing BCS, with 29.4% incidence of abortion and 33.3% perinatal mortality [7,8,10-13]. Women with pre-existent varices have up to a 25% risk of developing an episode of variceal hemorrhage during pregnancy, with the greatest risk in the second trimester and during delivery [2,3,14]. Varices should be treated with beta-blockers or band ligation [4,7,13,15]. While beta-blockers do confer a risk of intra-uterine growth restriction (IUGR), fetal and neonatal bradycardia, and neonatal hypoglycemia, benefits are deemed to outweigh these risks [7,16-20]. The aim of this study was to present a case of pregnant women with non-cirrhotic variceal bleeding due to BCS in the early second trimester.

Case

A pregnant woman at 13–14 weeks gestation presented to Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia on April 29, 2023 with profuse hematemesis, approximately 300 cc. The patient also defecated fishy-scented dark red stool once within 24 hours. A week ago, the patient was admitted for a four-day stay at Tgk. Chik Ditiro General Hospital, Sigli, Aceh, Indonesia due to similar complaints. The patient was given a transfusion of three packed red cells equivalent to 750 cc. Symptoms include pallor and fatigue since the first day of admission. The patient has no history of alopecia, arthralgia, repetitive aphthous ulcers, hypertension, diabetes mellitus, or alcohol consumption. The patient had a history of upper right quadrant abdominal pain a year ago. Abdominal ultrasonography (USG) on June 2022 revealed hepatomegaly with dilated hepatic veins. Gastroesophageal endoscopy on February 2023 revealed grade IV esophageal varices and grade IV gastric varices (**Figure 1**). Endoscopic band ligation was not performed due to the high risk of intraprocedural bleeding. The patient regularly took propranolol 10 mg twice a day and was on a soft diet.

Initial assessment showed the airway was patent and breathing was clear. The extremities were warm. The patient was fully conscious, Glasgow coma scale (GCS) scored 15 (E4V5M6), blood pressure 100/60 mmHg, pulse rate 92 bpm, respiratory rate 20 breaths per minute, body temperature 36.6^{o}C, oxygen saturation 98% in room air. The patient was 155 cm in height and body mass of 40 kg, with body mass index (BMI) of 16.6 kg/m^2 (underweight). Physical examination revealed bilateral conjunctival pallor, mucosal pallor, and non-icteric sclera. Jugular venous pressure was normal. Thorax and abdominal examination were within normal limits and extremities were pale but non-edematous. The electrocardiogram showed normal results.

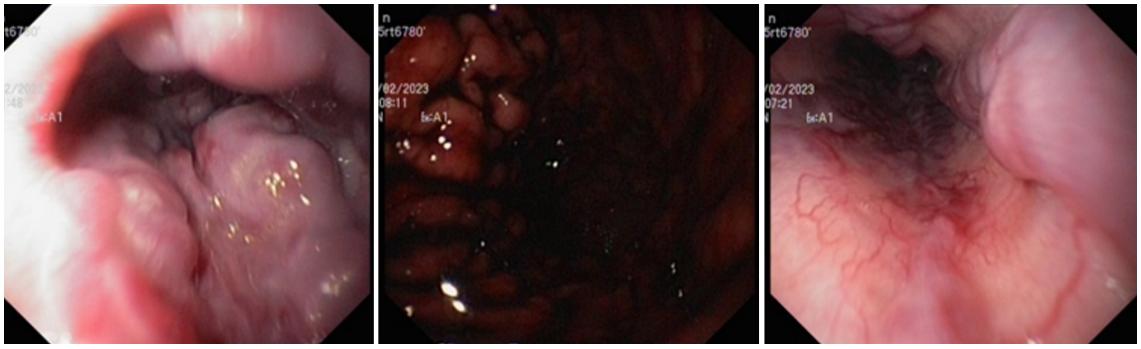

Figure 1. Gastroesophageal endoscopy shows grade IV esophageal varices and grade IV gastric varices.

Initial laboratory examination on April 2023 revealed extremely low hemoglobin (Hb) level (5.2 g/dL), low hematocrit level (16.0%), low erythrocyte count (2,000,000/mcL), leukopenia (3,490/mcL), thrombocytopenia (79,000/mcL). Erythrocyte revealed microcytic hypochromic anemia. The red cell distribution width was elevated. Hemostasis status showed bleeding tendency with lengthened PT (>90.0 s), elevated INR (>6.0), and lengthened activated partial-thromboplastin time (APTT) (>180.0 s; 5.53 times higher than normal reference). There was a marked elevation of D-dimer (2,310 ng/mL). Fibrinogen level was high (>500 mg/dL; 1.86 times higher than normal reference). Hepatitis serology was negative for both hepatitis B and hepatitis C. Liver function laboratory results were total bilirubin 0.42 mg/dL; direct bilirubin 0.12 mg/dL; indirect bilirubin 0.30 mg/dL; aspartate aminotransferase (AST) 22 U/L; alanine aminotransferase (ALT) 25 U/L. Total protein and albumin levels were low, 5.80 g/dL and 3.10 g/dL, respectively. Meanwhile, globulin level remained normal (2.70 g/dL) and random blood glucose 81 mg/dL. Renal function was normal (ureum 15 mg/dL, creatinine 0.5 mg/dL). An electrolyte test revealed slight hyperchloremia (115 mmol/L). Meanwhile, sodium and potassium levels remained normal at 133 mmol/L and 3.80 mmol/L, respectively.

In June 2022, USG revealed hepatomegaly, increased echogenicity of liver parenchyma, and dilation of hepatic veins. There were no splenomegaly, no gallbladder wall thickening, and no free fluid. Both kidneys and pancreas were normal. Meanwhile, recent USG findings (May 2023) were as follows: no hepatomegaly, the liver showed homogenous parenchyma, with coarse echogenicity, hepatic nodules (-), and no visible dilation of portal and hepatic veins. There was no visible dilation of intrahepatic and extrahepatic biliary ducts. There was no gallbladder enlargement, no gallstones nor sludge. However, pericholecystic fluid collection and gallbladder wall thickening were visible. There was splenomegaly (spleen length 15.17 cm) with homogenous parenchyma and no visible dilation of splenic veins. Pancreas and paraaortic lymph nodes were within normal sizes. Both kidneys and bladder were normal. Obstetric ultrasound revealed an intrauterine gestational sac with a viable fetus, and a fetal heart rate was detected. Free fluid was detected in the perihepatic, perisplenic, Morrison's pouch, and splenorenal recess with no visible effusion. Spectral Doppler revealed normal tracing flow of portal veins and hepatic arteries. Identification of hepatic veins was challenging. The FibroScan result confirmed mild hepatic fibrosis with liver stiffness of 8.4 kPa. Based on the clinical findings, the patient was diagnosed with BCS.

The patient was given a transfusion of three packed red cells (PRC) within three days until the Hb levels reached 9.0 g/dL. A routine laboratory test was performed immediately post-transfusion. Transfusion successfully elevated Hb (8.3 g/dL), hematocrit (25.0%), and erythrocyte count (3,000,000/mcL). The red cell distribution width was reduced to 15.2%. However, leukopenia (3,190/mcL) and thrombocytopenia (69,000/mcL) remained unresolved. The differential cell count was similar to the initial laboratory test. Seven days post-transfusion, repeated laboratory results showed a slight improvement in Hb (8.5 g/dL), APTT improved to normal (30.30 s), PT improved to normal (14.4 s), INR was back in the normal range (1.01). There was a decline in fibrinogen (243 mg/dL), marked elevation of D-dimer (3010 ng/mL), and platelet count remained low (61,000/mcL). Renal function test showed low serum creatinine (0.48 mg/dL) and low ureum (5.0 mg/dL). Electrolyte test revealed normal serum Na^+ (138 mmol/L)

and K^+ (3.7 mmol/L), while serum Ca^{2+} was borderline low (8.6 mmol/L). Serum Cl^- remained high (113 mmol/L).

Besides transfusion, the patient was put on bed rest. An intravenous (IV) line was established and the patient was given an IV Ringer lactate drip. IV octreotide bolus 0.2 mg was administered and proceeded the following three days with a continuous drip of 0.2 mg octreotide diluted in 50 cc of NaCl 0.9% with an infusion rate of 6.25 cc/hour. The patient was also given an IV 10 mg vitamin K injection every eight hours, IV 500 mg tranexamic acid injection every eight hours. Per-oral treatments include lactulac syrup two tsp t.i.d., folic acid 0.4 mg b.i.d., ferrous sulfate 30 mg t.i.d., and Curcuma 20 mg t.i.d. On the third day of inpatient, measured vital signs were as follows: blood pressure 100/60 mmHg, pulse rate 90 bpm, respiratory rate 20 breaths per minute, and body temperature of 36.5 ^oC. Propranolol had not been given since the pulse rate was still above 80 bpm. Propranolol 10 mg can be given twice a day once the patient reaches hemodynamic stabilization (blood pressure >90/60 mmHg and pulse rate <80 bpm). The patient was given a soft diet of 1,700 kcal per day in the form of hepatosol 200 cc six times a day.

Discussion

BCS is a rare post-hepatic cause of portal hypertension with an incidence of 0.35–2.5 cases per 100.000 population and 1.0 % happened in pregnancy [2,8]. Hepatic venous outflow obstruction eventually causes liver fibrosis. In pregnancy, obstruction of hepatic veins occurs usually due to thrombosis [2,8]. However, the size of the gravid uterus can also cause stenotic effects on central veins [1,11]. Women with BCS are at risk of developing severe exacerbation of their underlying disease during pregnancy due to elevated blood estrogen levels, elevated levels of pro-coagulant factors, decrease in natural anticoagulants, reduction in fibrinolysis due to a decrease in t-PA activity, increased circulating blood volume, and gravid uterus compressing inferior vena cava [2,8,11,18].

Although only a minority of women with BCS become cirrhotic, variceal bleeding can still happen due to portal hypertension [2,8]. Variceal bleeding is the most fatal complication in pregnancy with co-existing BCS, with 29.4% incidence of abortion and 33.3% perinatal mortality [2]. Women with pre-existent varices have up to a 25% risk of developing an episode of variceal hemorrhage during pregnancy, with the greatest risk in the second trimester and during delivery [2,8]. Pregnancy should have been postponed using non-hormonal contraceptives until gastroesophageal varices are ligated and portal hypertension is under control, either medically by non-selective beta-blockers (NSBB) or surgically by a transjugular intrahepatic portosystemic shunt (TIPS) [6,8,29].

This patient experienced profuse hematemesis and dark-bloody stool, indicating active upper gastrointestinal bleeding. Pallor and fatigue were signs of anemia due to chronic blood loss and was treated with a blood transfusion. The patient's gastroesophageal endoscopy results revealed grade IV esophageal varices and grade IV gastric varices, in which grade III-IV varices were classified as varices needing treatment (VNT) due to their high risk of rupture, making the patient a candidate for NSBB treatment or endoscopic band ligation (EBL) [3,30,31]. Current guideline recommends EBL as the gold standard endoscopic treatment after hemodynamic stabilization [3,6]. Based on the laboratory results, Child-Turcotte-Pugh (CTP) score was 8 (Child-Turcotte Class B, accounted for 30% perioperative mortality in abdominal surgery) and as the risk of 30-day post-EBL re-bleeding was higher in larger varices, EBL was not performed [2,3,30]. Moreover, thrombocytopenia, elevated INR, and hypofibrinogenemia exposed patients to a higher risk of intraprocedural bleeding [30,31].

The patient was also given low-dose NSBB propranolol 10mg b.i.d. throughout early pregnancy. On the other hand, administering NSBB (carvedilol, propranolol) to alleviate portal hypertension was not recommended due to risks of neonatal bradycardia, hypoglycemia, and intrauterine growth retardation (pregnancy category C) [3,4,6,26]. Only animal studies have been performed regarding the safety of propranolol. Rat studies showed embryotoxicity at doses exceeding 150 mg/kg/day [26]. Because of safety concerns, low-dose propranolol was given under strict fetal monitoring. Regular antenatal check-ups showed neither fetal death nor growth restriction.

Ideally, patients non-qualified for NSBB should have used TIPS to control portal hypertension [3,6]. Patients classified as Child-Turcotte Class B or C with active bleeding on endoscopy are were candidates for the TIPS procedure [3,6,7]. This procedure is ideally performed within 72 hours of admission [3]. A catheter will be inserted through the jugular vein to hepatic veins under the guidance of fluoroscopy and a bypass to the inferior vena cava was created. A newly devised radiation-sparing maneuver reduces anticipated fetal radiation exposure to 5.49 mSv, TIPS effectively resolves portal hypertension with minimum radiation risk to the fetus, hence its popularity as 'salvage therapy' [6,13,25]. However, Glasgow-Blatchford Bleeding Score (GBS) score was 10, indicating high-risk gastrointestinal bleeding with >50% risk of requiring medical interventions, i.e. transfusion, endoscopy, or surgery [2] and the Rockall score was 5 (high-risk upper GI bleeding), accounting for 24.1% re-bleeding risk and 10.8% mortality [2]. As a result, TIPS was not chosen for the patient due to its invasiveness.

Since portal hypertension is the main etiology of gastroesophageal variceal bleeding, several imaging modalities have been developed to measure its severity. The severity of portal hypertension was reflected by HVPG, which is the difference between pressures of the hepatic vein and vena cava [2,12,16,19]. Measurement of HVPG can be done using Doppler USG, MR venography, and CT venography. Unfortunately, CT is contraindicated in pregnancy due to teratogenic radiation exposure. MRI is another radiation-free option, yet costly. Unlike venography, Doppler USG becomes the best imaging modality due to its safety and minimally invasive [16].

Pathognomonic signs of portal hypertension in Doppler USG include biphasic or reverse flow in the portal vein (late stage) and enlarged paraumbilical veins. Non-specific signs include dilated portal vein (>13 mm), appearance of collateral vessels/varices, splenomegaly, and ascites [19,21]. The patient's initial USG revealed hepatomegaly and dilation of hepatic veins. Development of collateral vessels or relief of venous obstruction may explain seemingly-resolved hepatomegaly on the last USG. A normal-sized liver showed homogenous parenchyma with coarse echogenicity indicating hepatic inflammation, with no visible dilation of the portal and hepatic veins. There seemed to be a disease escalation since the current USG revealed new findings of splenomegaly, ascites, and gallbladder wall thickening. Spleen length was 15.17 cm and there was free fluid in the perihepatic, perisplenic, Morrison's pouch, and splenorenal recess. There were pericholecystic fluid collection and gallbladder wall thickening, indicating reactive cholecystitis toward liver inflammation.

The severity of portal hypertension was reflected by the extent of hepatic fibrosis. Hence the capability of fibroscan to substitute measurement of HVPG by invasive venography [3,17,23]. The HVPG (mmHg) is equal to 7.4 + 0.204*liver stiffness (kPA) [23]. The Fibroscan result confirmed mild hepatic fibrosis with liver stiffness of 8.4 kPa, indicating a pre-existing liver disease. Calculation using the above-mentioned equation yielded HVPG 9.11 mmHg (clinically insignificant portal hypertension).

For predicting the presence of gastroesophageal varices, gallbladder wall thickness (GBWT) can be measured on USG. Thus, GBWT complemented upper GI endoscopy as a standard diagnostic test for gastroesophageal varices. A study mentioned a cutoff value of the gallbladder wall thickness of >3.5mm accurately predicts the presence of grade III-IV gastroesophageal varices with 45% sensitivity, 90% specificity, 64.3% PPV, 80.4% NPV, and 77.1% accuracy [24]. In this patient, GBWT was 10.7 mm, strongly indicating the presence of high-grade gastroesophageal varices.

First management of variceal hemorrhage includes securing the airway and nasogastric tube decompression should be performed [3,10,13,25]. Oxygen supplementation is given as indicated. Blood pressure, heart rate, and respiratory rate should be closely monitored to estimate the severity of blood loss for transfusion. The patient was administered IV Ringer lactate drip, but the pulse rate did not exceed 100 bpm, therefore estimated blood loss was less than 15% of total blood volume, classified as grade 1 hemorrhagic shock. Aggressive crystalloid loading is currently frowned upon to prevent dilutional coagulopathy [3,10]. Body temperature should be kept warm by putting the patient underneath a heated blanket since hypothermia inhibited hemostatic function [3,10]. Additionally, the current guideline recommends the administration of broad-spectrum antibiotics in acute variceal bleeding due to the great risk of infection [3,14].

In addition to initial resuscitation, PRC transfusion was given to the patient until the Hb levels reached 9.0 g/dL. Current guidelines recommended PRC transfusion only for Hb <7 g/dL since liberal use of PRC transfusion significantly increased the mortality rate in patients [3,9,13,14,25]. Hb levels are to be maintained at 7–9 g/dL [3]. In contrast to PRCs, transfusion of platelets, the use of fresh frozen plasma, or administration of recombinant factor VIIa to correct platelet count or INR, respectively, did not demonstrate a clear benefit and is therefore not recommended [3,14].

Splanchnic vasoconstrictors are recommended for upper GI bleeding caused by portal hypertension. Octreotide falls under the category of somatostatin and analogs. The possible adverse effect includes intrauterine growth restriction due to a strong vasoconstrictive effect that disrupts fetoplacental circulation [9,15,26]. A few spontaneous abortions had been reported during the early trimester. However, the administration is allowed as long as the benefits outweigh the risks (pregnancy category B). The dose for acute variceal hemorrhage is 50 µg IV bolus followed by 50 µg/hour IV infusion for two to five days [26]. If hemorrhage is not controlled in the first hour, octreotide bolus can be repeated. The patient was administered IV octreotide and to monitor adverse effects, such as cardiac dysrhythmia, EKG should be performed. Other somatostatins i.e. vasopressin (pregnancy category C) and terlipressin (pregnancy category N/A) are not recommended due to their strong vasoconstrictive properties. These drugs disrupt uteroplacental circulation, potentially causing spontaneous abortion and placental abruption [26].

Additionally, 500–1,000 mg of IV tranexamic acid (pregnancy category B) can be administered, followed by infusions of 100 mg over eight hours repeatedly for 24 hours [26]. This patient was given 500 mg of IV tranexamic acid injection every eight hours. Vitamin K injections are classified into the pregnancy category N/A, with some embryotoxicity in animal studies. The administration is allowed as long as the benefit outweighs the risk. This patient was given 10 mg of IV vitamin K injection every eight hours due to the pathophysiology of bleeding in chronic liver disease, which depletes vitamin K-dependent coagulation factors [26]. For gastric mucosal protection, antacids are not recommended because they reduce serum concentrations of octreotide [26]. Sucralfate (pregnancy category B) or proton-pump inhibitors, except omeprazole (pregnancy category C), is preferred [6,26]; the patient was given lactulac syrup.

It is ideally performed within 12 hours since bleeding is detected. Since the onset of upper GI bleeding was >12 hours from admission time, EBL was not performed. The EBL procedure was scheduled one month later after the patient's condition was declared stable.

Conclusion

The management of non-cirrhotic variceal bleeding in pregnancy requires a multidisciplinary approach, involving resuscitation, medical therapy, endoscopic interventions, and, in severe cases, TIPS placement. Regular monitoring of both the mother and the fetus is crucial for optimal outcomes. Individualized care must be provided, considering the risks and benefits of each intervention for both the mother and the developing fetus.

Ethics approval

The patient provided written informed consent to be published as a case report.

Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

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References

1. Sharma A, Keshava SN, Eapen A, *et al.* An update on the management of Budd–Chiari syndrome. Digest Dis Sci 2021;66:1780-1790.
2. Li Y, De Stefano V, Li H, *et al.* Epidemiology of Budd-Chiari syndrome: A systematic review and meta-analysis. Clin Res Hepatol Gastroenterol 2019;43(4):468-474 .
3. Pfisterer N, Unger LW, Reiberger T. Clinical algorithms for the prevention of variceal bleeding and rebleeding in patients with liver cirrhosis. World J Hepatol 2021;13(7):731-746.
4. Park C, Patel YA, Suhocki P, *et al.* High-risk third trimester pregnancy with decompensated cirrhosis safely delivered following emergent preoperative interventional radiology for mitigation of variceal bleeding. Clin Imaging 2020;1(68):143-147.
5. Tolunay HE, Aydin M, Cim N, *et al.* Maternal and fetal outcomes of pregnant women with hepatic cirrhosis. Gastroenterol Res Pract 2020;2020:5819819.
6. Mikolasevic I, Filipec-Kanizaj T, Jakopcic I, *et al.* Gastrointestinal and other hepatic disorders in pregnancy (related liver disorders), dysfunction in pregnancy. World J Case Rep Clin Img 2022;1(1):1-6.
7. Faulkes RE, Chauhan A, Knox E, *et al.* Review article: Chronic liver disease and pregnancy. AP&T 2020;52:420-9.
8. Hernández-Gea V, De Gottardi A, Leebeek FWG, *et al.* Current knowledge in pathophysiology and management of Budd-Chiari syndrome and non-cirrhotic non-tumoral splanchnic vein thrombosis. J Hepatol 2019;71(1):175-199.
9. Giri S, Sahoo S. Pregnancy in patients with non-cirrhotic portal hypertension: A literature review. Rev Bras Ginecol Obstet 2022;44(6):609-613.
10. Dokmak A, Trivedi HD, Bonder A, Wolf J. Pregnancy in chronic liver disease: Before and after transplantation. Ann Hepatol 2021;26:100557.
11. Wiegers HMG, Hamulyák EN, Damhuis SE, *et al.* Pregnancy outcomes in women with Budd–Chiari syndrome or portal vein thrombosis – a multicentre retrospective cohort study. BJOG 2022;129(4):608-617.
12. Cheng Q, Tree K. Systematic review of thrombolysis therapy in the management of non-cirrhosis-related portal vein thrombosis. World J Gastrointest Surg 2021;25(6):1579-1590.
13. Stelmach A, Słowik Ł, Cichoń B, et al. Esophageal varices during pregnancy in the course of cirrhosis. Eur Rev Med Pharmacol Sci 2020;24(18):9615-9617.
14. Keepanasseril A, Gupta A, Ramesh D, *et al.* Maternal–fetal outcome in pregnancies complicated with non-cirrhotic portal hypertension: Experience from a tertiary centre in south india. Hepatol Int 2020;14(5):842-849.
15. Rahim MN, Pirani T, Williamson C, Heneghan MA. Management of pregnancy in women with cirrhosis. United European Gastroenterol J 2021;9(1):110-119.
16. Aitcheson G, Cezar C, John I, John B V. Update on the evaluation and management of portal hypertension. Gastroenterol Hepatol (N Y) 2021;17(12):569-578.
17. Gelman S. Novel imaging and serum biomarkers for the diagnosis of liver fibrosis and portal hypertension. Lithuanian University of Health Sciences 2020.
18. Mishra VV, Mahalingam MA, Solanki SB, Aggarwal R. Management of pregnancy in a rare case of Budd-Chiari syndrome: A case report. J SAFOG 2022;14(4):475-476.
19. Xie W. Consensus for management of portal vein thrombosis in liver cirrhosis (2020, Shanghai). J Dig Dis. 2021;(4):176-186.
20. Augustine A, John R, Simon B, *et al.* Imaging approach to portal hypertension. J Gastrointestinal Abdominal Radiol 2023;6:123-137.
21. Tong Y, Zhang M, Qi Z, *et al.* Hepatic venous occlusion type of budd–chiari syndrome versus pyrrolizidine alkaloid-induced hepatic sinusoidal obstructive syndrome: A multi-center retrospective study. J Pers Med 2023;13(4):603.

22. Danielsen KV, Hove JD, Nabilou P, *et al.* Using MR elastography to assess portal hypertension and response to beta-blockers in patients with cirrhosis. Liver Int 2021;41(9):2149-2158.
23. Sánchez-Conde M, Miralles P, María Bellõn J, *et al.* Use of transient elastography (FibroScan®) for the noninvasive assessment of portal hypertension in HIV/HCV-coinfected patients. J Viral Hepat 2011;18(10):685-691.
24. Elkerdawy M, Ahmed M, Zaghloul M, *et al.* Does gallbladder wall thickness measurement predict esophageal varices in cirrhotic patients with portal hypertension? Eur J Gastroenterol Hepatol 2021;33(6):917-925.
25. Juan MRJ, Castro-Villegas F, Carmen EOB. Modified sugiura procedure: An alternative for non-cirrhotic patients with extrahepatic portal vein thrombosis and recurrent variceal bleeding. Rev Colomb Gastroenterol 2020;35(3):377-381.
26. Wu GY, Mavilia MG, George, Wu Editors Y. Clinical gastroenterology series editor: Pocket Handbook of GI Pharmacotherapeutics 2021.
27. Wada H, Matsumoto T, Yamashita Y. Diagnosis and treatment of disseminated intravascular coagulation (DIC) according to four DIC guidelines. J Intensive Care 2014;2(1):15.
28. Sharma S, Sharma P, Tyler LN. Transfusion of blood and blood products: Indications and complications. Am Fam Physician 2011;83(6):719-724.
29. Habash M, Murray A, Heeke B, *et al.* Outcomes of transjugular intrahepatic portosystemic shunt using 12 mm diameter polytetrafluoroethylene covered stents in cirrhotic patients with portal hypertension. Diagn interv imaging 2022;28(3):239-243.
30. Drolz A, Schramm C, Seiz O, *et al.* Risk factors associated with bleeding after prophylactic endoscopic variceal ligation in cirrhosis. Endoscopy 2021;53(3):226-234.
31. Zhang H. A novel risk scoring system for predicting variceal oesophageal and gastric bleeding in patients with cirrhosis and the tailored nursing care delivery based on the assessment. J Med Health Sci 2022;11(4):47-53.