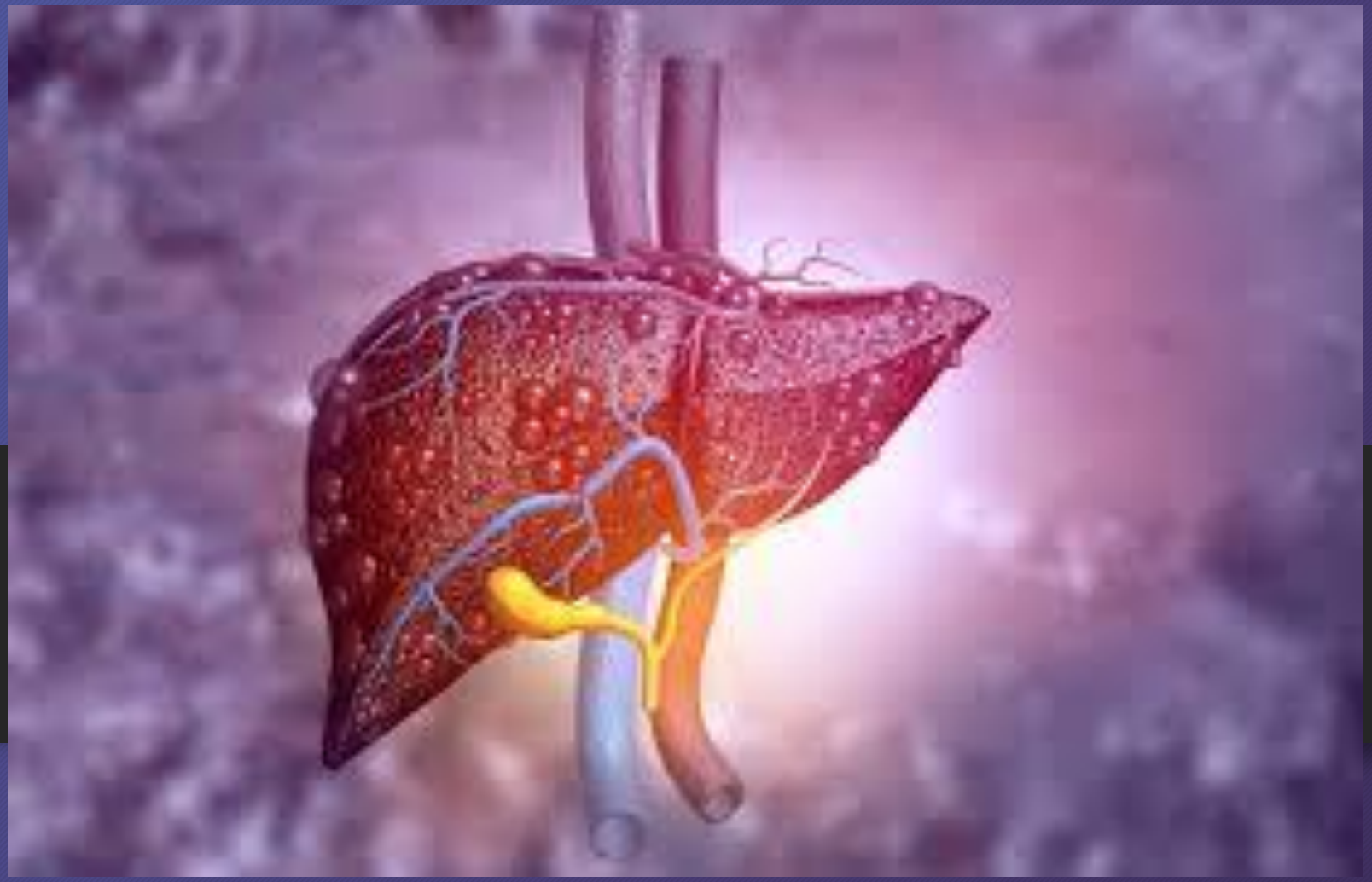

Cirrhosis and pregnancy

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cirrhosis

- Pregnancy is a rare event in women with liver cirrhosis
- The prevalence of cirrhosis in women of reproductive age is 0.045%.

The incidence of cirrhosis in pregnancy is reported as approximately 1 per 4500 pregnancies .

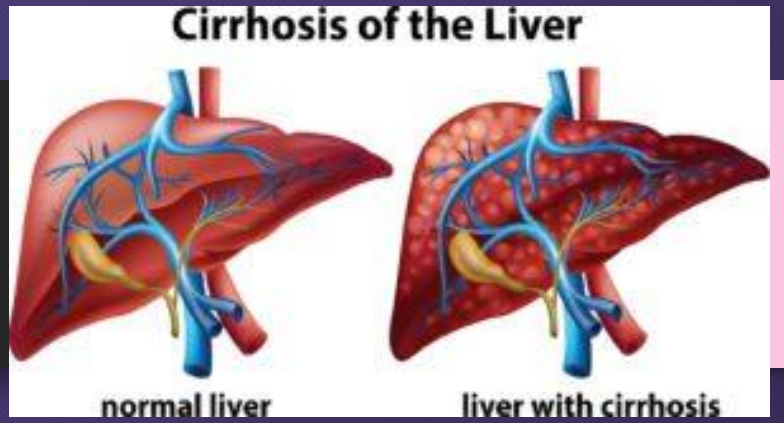
the most common causes of liver cirrhosis in women:

viral hepatitis, autoimmune hepatitis, alcoholic liver disease and non-alcohol related fatty liver disease.

more frequent in the last decades.

the effects of liver cirrhosis on the course of pregnancy and the effects of pregnancy on underlying cirrhosis are both of importance.

Physiological changes during pregnancy



- Portal HTN : a hyper-dynamic circulation, low systemic vascular resistance and elevated portal venous pressures (10 mmHg). **This process is exaggerated during pregnancy.**
- Rapidly increasing blood volume during the second trimester(renin–angiotensin system activation), increased aldosterone production and sodium/water retention.
- Due to maternal blood volume expansion, augmented cardiac output and increased compression of the gravid uterus on the inferior vena cava, portal pressures rises

- Portal pressure peaks during the second trimester, increasing the risk of VH. Progesterone and estrogen during pregnancy and influencing hepatic metabolism, synthesis and excretory function
- Most liver parameters remain stable during pregnancy, other than alkaline phosphatase and alphafetoprotein which rise during pregnancy because of foetal/placental production.
- Albumin tends to reduce during pregnancy.

Pre-pregnancy counselling

- Women with cirrhosis should therefore receive prepregnancy counselling with a team of experts

- This facilitates tailored medication regimens and triage of patients by risk profile in addition to anticipation of complications.
- Patients with cirrhosis are often malnourished. If there are concerns regarding nutrition pre-pregnancy or antenatally, early referral to a dietician can prove beneficial.

Infertility in cirrhosis

- Fertility is decreased in women with cirrhosis due to disruption of the hypothalamic–pituitary axis combined with impaired hepatic metabolism of sex hormones, porto-systemic shunting of weak androgens and peripheral aromatisation of androgens.
- Menstrual irregularities can lead to unexpected pregnancies in these women. Others may seek assisted conception, for example in vitro fertilization, which is not without risk.

Risk stratification

- Pregnancy outcomes are related to the severity of underlying maternal liver disease.
- Pre-conception MELD scores <6 predict positive outcomes with minimal complications, whilst MELD scores >10 predict hepatic decompensation during pregnancy. These patients should be carefully counselled about the possible risks of decompensation, liver transplantation (LT) and death during pregnancy.

- Furthermore, a pre-conception albumin–bilirubin score of <-2.7 (ALBI grade 1) has been demonstrated to predict live birth, and a preconception aspartate AST-to-platelet ratio index of 0.84 predicts term pregnancies

MELD score =
$3.78 \times \mathrm{Ln}(\mathrm{TBiL}\ \mu mol/L) + 11.2 \times \mathrm{Ln}(\mathrm{INR}) + 9.57 \times \mathrm{Ln}(\mathrm{creatinine}\ mg/dL) + 6.4$

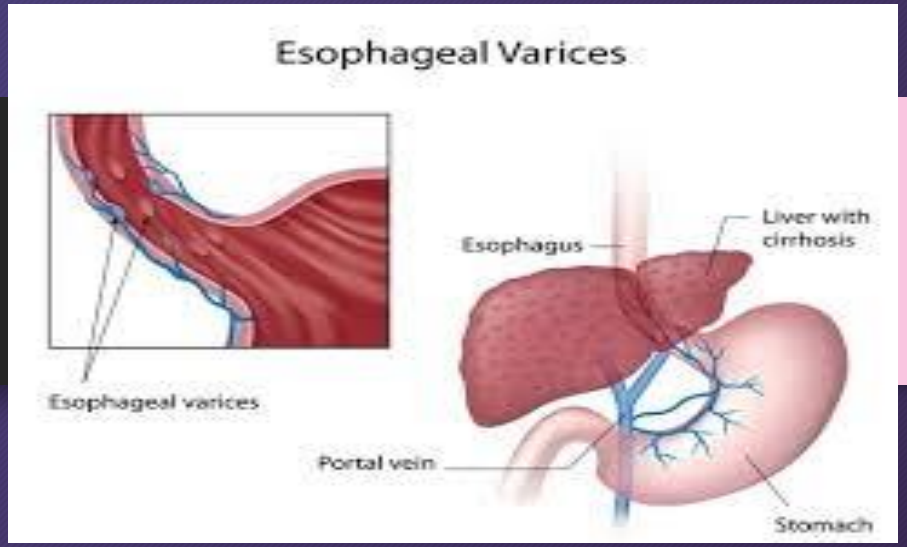
ALBIscore =
$-0.085 \times (\mathrm{albumin}\ g/L) + 0.66 \times \lg(\mathrm{TBil}\ \mu mol/L).$

arameter	Assign 1 point	Assign 2 points	Assign 3 point
scitis	Absent	Slight	Modera
ilirubin (mg/dL)	< 2	2-3	>3
lbumin (g/dL)	>3.5	2.8-3.5	<2.8
rothrombin time econd over ntrol) or NR	<4 <1.7	4-6 1.7-2.3	>6 >2.3
ncephalopathy	None	Grade 1-2 (Mild to moderate)	Grade 3- (Severe

Maternal complications
Hepatic decompensation

- Up to 25% of women with cirrhosis may experience decompensation (mostly VH) during pregnancy.
- However, a recent retrospective population-based study from North America suggests that the rate may be lower at 1.6%.
- History of pre-pregnancy hepatic decompensation may significantly increase the risk (13%) of decompensation during pregnancy

Variceal Hemorrhage



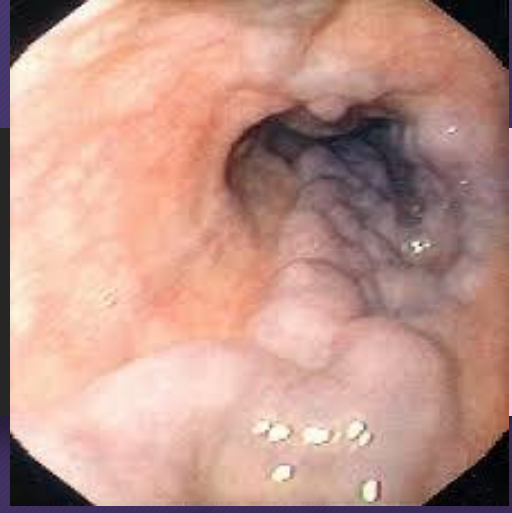
VH has been reported in up to one third of pregnant women with cirrhosis and half with PHTN. Among those with preexisting varices upto78% will have GIB during pregnancy

Associated mortality was up to 50% in older studies, although recent series suggest rates <20%

in women with non-cirrhotic PHTN, mortality is only 2–6% (better liver function).

- The American College of Gastroenterology recommends variceal screening in the second trimester in pregnant women with suspected PHTN.
- Some experts also advocate pre-conception surveillance.
- Platelets <110 cells/L may predict the presence of varices in the second trimester.
- In patients with significant PHTN and intra-abdominal varices, magnetic resonance imaging may reveal pelvic varices, which is important to know when considering mode of delivery.

Endoscopy



With a few stipulations, OGD can be performed safely in pregnant women(**fetal hypoxia from sedative drugs or poisioning**).

In late pregnancy, aorto-caval compression in the supine position can cause reduced venous return, cardiac output and uteroplacental blood flow. Left lateral positioning avoids this.

Despite a FDA pregnancy category of D, in practice, midazolam is used widely during endoscopy in pregnant women, without significant consequences.

Over-sedation (benzodiazepines/opiates) can cause materno-fetal hypotension/hypoxia.

Guidelines suggest that meperidine (pethidine) and propofol can be used with relative safety in pregnant women.

Management

- In acute VH during pregnancy, broad-spectrum antibiotics should be initiated. Use of terlipressin is controversial; its vasoconstrictive properties may induce uterine contractions, with decreased uterine blood flow leading to ischaemia, which can subsequently result in spontaneous abortion and placental abruption myocardial infarction and hypertention. It should only be used in cases when endoscopic therapy has failed.
- Octreotide may be a suitable alternative

- EBL remains the mainstay of therapy for acute VH. Sclerotherapy has previously been used successfully, but potential shunting of toxic material to the placenta remains concerning. Prospective studies comparing these two methods in pregnancy are lacking, although EBL is superior in the non-pregnant population.
- In those with refractory bleeding despite optimal endoscopic therapy, rescue TIPSS insertion can successfully control bleeding. In this situation, the benefits of performing this procedure are likely to outweigh the risks

- TIPS is generally contraindicated(risk of radiation)
- Portal-vein flow usually increases during pregnancy, although the impact of pregnancy on TIPSS function is unknown. In women with previous TIPSS, regular (frequency unclear) ultrasound monitoring of the shunt during pregnancy is recommended.
- A few case reports have described ongoing TIPSS patency during pregnancy, with possible increased flow velocity in the portal vein, stent and hepatic artery.

- If varices are identified, prophylactic EBL to prevent VH remains controversial, but is practiced in some centers.

- Primary prophylaxis with non-selective beta-blockers may be beneficial but should be balanced with risks(women at high risk for bleeding);IUGR,neonatal hypogelycemia and bradycardia

Hepatic encephalopathy

- Similar principles apply to managing HE during pregnancy, although certain medications should be avoided where possible.
- At delivery, the presence of HE may influence the administration of anaesthesia, as certain drugs may precipitate hypotension and worsen HE.

Ascites and SBP

Ascites is relatively rare (7–11%) during pregnancy(increased intraabdominal pressure).

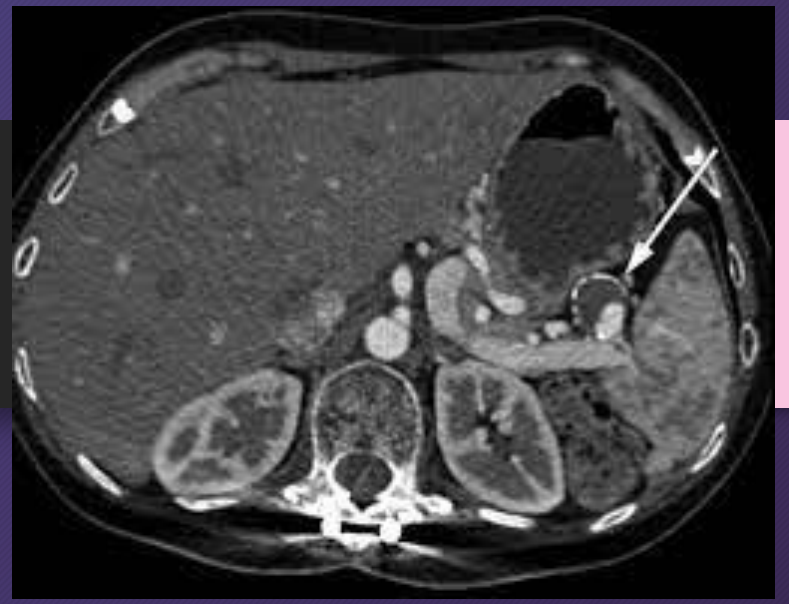
If treatment is required, Na restriction and duretic use

If spontaneous bacterial peritonitis is confirmed, management includes antibiotics and human albumin solution.

- It is important to consider alternative etiologies of intra-abdominal infection, as secondary peritonitis

. Prophylactic antibiotics (norfloxacin/ciprofloxacin) should be avoided during pregnancy if possible, but can be used safely during breastfeeding, provided the infant is monitored for side effects (diarrhea/ candidiasis)

Splenic artery aneurysm rupture



- Spontaneous rupture of a splenic artery aneurysm (SAA) is rare(2.6%). Risk is greatest in pregnant women with cirrhosis and PHTN in the third trimester(70%) due to increased splenic blood flow from a hyper-dynamic circulation and estrogen effect.
- Symptoms include abdominal pain and syncope. A curvilinear calcification in the left upper quadrant on imaging may represent a SAA. Up to 25% of patients experience the ‘double rupture phenomenon’: warning symptoms from an initial small self-contained rupture, which hours later results in significant rupture with rapid intra-abdominal bleeding and haemorrhagic shock. Materno-foetal mortality rates are high (70–95%) in these cases

- Trans-catheter embolisation is now the mainstay of treatment in cases of rupture,
- surgical intervention (ligation,splenectomy) reserved for failed therapy or when interventional radiology is unavailable.
- Prophylactic intervention can be considered if a SAA has previously ruptured or if a large aneurysm (>2–3 cm) has been identified pre-conception

Malignancy

- Hepatocellular carcinoma (HCC) in pregnancy is rare. Hyperestrogenaemia and increased vascularity has been postulated to accelerate HCC progression during pregnancy, but data are inconsistent.
- alpha-fetoprotein cannot be used as a marker of HCC during pregnancy.
- HCC in pregnancy has been associated with poorer obstetric outcomes, with a 12.5% risk of spontaneous rupture and inferior maternal survival rates.
- Trans-arterial embolisation, radiofrequency ablation and surgery are all possible during pregnancy, although careful consideration of risk versus benefit must occur in a multidisciplinary setting.

Maternal outcomes

Death rates in pregnant women with cirrhosis range from 0% to 14%; older studies report higher rates, while newer ones report rates <2%. Women with cirrhosis are more likely to have prepregnancy co-morbidities (e.g. diabetes, hypertension, obesity and dyslipidaemia) when compared to the general population.

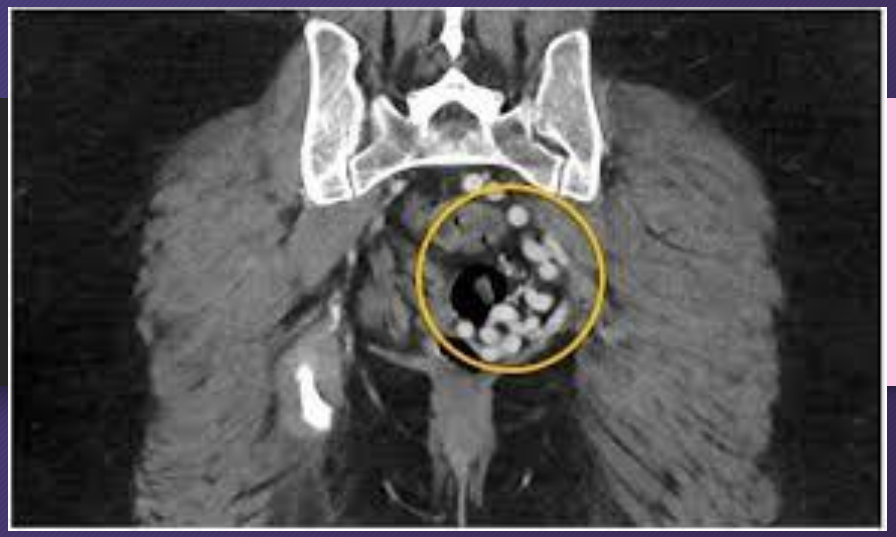
- Rates of pregnancy-induced hypertension (PIH) range widely between 5.4% and 21.5% in various studies.
- It is difficult to interpret whether rates (3.9–13.5%) of pre-eclampsia are greater in pregnant women with cirrhosis.
- Studies have shown no significant difference in rates of gestational diabetes in pregnant women with cirrhosis compared to background risk.
- Intrahepatic cholestasis of pregnancy is more common in women with cirrhosis.

Fetal outcomes

- Live birth rates in pregnancies of women with cirrhosis are poorly reported, with rates varying between 58% and 100%.
- Rates of neonatal death are between 0% and 8.3%, and are believed to be greater than the general population(related to prematurity/LBW).
- Stillbirth rates range between 1% and 8%.
- Congenital malformation rates (0.4–2%) are comparable to the general population.

Delivery

- An area of controversy in women with PHTN is approach to delivery. Concerns arise from excessive straining and repeated Valsalva manoeuvres during labour, which change intra-abdominal/portal pressures and may precipitate VH. There are no recent studies evaluating the impact of vaginal delivery on the risk of VH. Consequently, many experts recommend an elective C-section or forceps delivery under extradural analgesia, which is not without risk and a vascular surgeon should be available.
- a C-section may require corrective products and pre-emptive surgical planning to avoid intraabdominal/ pelvic varices. Furthermore, women with cirrhosis may experience poor wound healing and infection.



- Post-partum haemorrhage (PPH) occurs in 7–10% of women with cirrhosis.
- due to a combination of factors: thrombocytopaenia, imbalance of coagulation factors and aberrant variceal formation.

Post-partum

- Women with cirrhosis should be able to breastfeed, provided they are not on contraindicated medications. Early advice on contraception should be given. Women with compensated cirrhosis have no limitations in their contraceptive options. However, those with decompensated cirrhosis are restricted to barrier methods and copper intrauterine devices. Other methods can be considered on an individualized basis after specialist discussion. A caveat to consider is the use of copper intrauterine devices in Wilson's disease, as the manufacturers list this condition as a contraindication.

Medication use

- Majority of medications fall into pregnancy category C(Lasix,spironolactone,propranolol,Ciprofluxacin,hydroxyzine)
- Azathioprine,penicillamine and neomycine D
- Octreotide,cefotaxime lactoluse, telbivudine,prednisolone and UDCA B

Pregnancy in women with liver cirrhosis is associated wit increased risk for complications: a systematic review an meta-analysis of the literature
March 19, 2021

Our search retrieved 3118 unique publications. After title and abstract screening, 130 studies were selected for full text eligibility screening. We included 11 studies (with 2901 pregnancies with liver cirrhosis) in the systematic review, of which 7 were eligible for the meta-analysis (Figure 1). The total number of pregnancies with liver cirrhosis included in the meta-analysis was 2685 as well as 4,283,173 pregnancies without liver cirrhosis (control group).

Conclusion

- Pregnancy in women with cirrhosis is not without risk, with increased rates of maternal mortality, VH, PIH and PPH, and increased rates of neonatal mortality, prematurity and LBW. Women should be offered PPC, which not only better informs the patient, but also allows the opportunity to prognosticate and predict outcomes, with the initiation of individualized therapies/monitoring during pregnancy. **Unfortunately, data are limited in the field, making accurate counselling problematic.**